#14

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTORNEY DOCKET NO.: 076333-0240

Applicant: Robert H. Getzenberg

Title: BLADDER CANCER NUCLEAR MATRIX PROTEINS, POLYNUCLEOTIDE SEQUENCES ENCODING THEM, AND THEIR USE

Application No.: 09/866,927

Filing Date: May 30, 2001

Examiner: Larry Ronald Helms

Art Unit: 1642

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
Box AF
Washington, D.C. 20231

Sir:

I, Robert H. Getzenberg, being duly warned, hereby declare and state:

1. That I am a citizen of the United States and reside at 1627 Augusta Drive, Pittsburgh, PA 15237-6702.

2. That I am the named inventor of the subject matter disclosed in the United States application Serial No. 09/418,839 ("the application").

3. That I am an Associate Professor at the University of Pittsburgh School of Medicine. I have been doing research and development in the field of nuclear matrix protein biology and tumor markers since 1987. Attached is my Curriculum Vitae to further explain my experience and background.

4. That I have understood the Examiner's position on page 4 of the Office Action, that there is a discrepancy in the molecular weight of the BLCA-6 protein. As evidenced by Getzenberg *et al.* (*Cancer Research* **56**:1690-94, 1996), the molecular weight of the BLCA-6 is 31-kD. However, the specification incorrectly states that it has a molecular weight of 22-kD.

5. That at the time of preparing the instant application and other related applications (parent application, U.S. Patent No. 5,866,535 and a related application, U.S. Patent No. 6,280,956), a clerical mistake was inadvertently made in disclosing the correct molecular weight of the human BLCA-6 protein. At the filing of the priority application, U.S. provisional application No. 60/006226, filed November 3, 1995), Applicant submitted a preprint (see enclosed copy) to his undersigned attorney at Foley & Lardner, to cover the instant invention. The preprint was received and stamped on October 18, 1995. As indicated at page 20, Table 2 of the preprint, the molecular weight of BLCA-6 protein was 22-kD. However, at page 21, Figure 1B, a silver stained 2-D electrophoresis gel depicted a BLCA-6 protein that was above the 29 kD molecular weight marker protein. This error was unnoticed by me or by my attorney.

6. I am writing this affidavit to stress that the molecular weight of the claimed human BLCA-6 protein is indeed 31-kD and that the correct molecular weight is an inherent property of the protein. One of ordinary skill in the art, upon following the procedural steps for collecting the samples and performing the protein separation described in the application as filed, would inherently obtain a protein having a molecular weight equal to about 31 kD. In fact, out lab has run this procedure with other bladder samples and always obtained a protein of 31-Kd. Accordingly, the 31-Kd molecular weight is an inherent property of the BLCA-6 protein that results from the above-mentioned techniques. This inherent property was shown in Figure 1B of the preprint and disclosed in the cited reference (Getzenberg et al., *Cancer Research* **56**:1690-94, 1996).

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Dated: _____

_____

Robert H. Getzenberg

CURRICULUM VITAE

BIOGRAPHICAL

Name:	ROBERT HOWARD GETZENBERG	**Birth Date:** March 12, 1965	
Home Address:	1627 Augusta Drive Pittsburgh, PA 15237-6702	**Birth Place:** Haverford, PA	
Home Phone:	(412) 366-9105	**Citizenship:** U. S. A.	
Business Address:	University of Pittsburgh Shadyside Medical Center Urology Research G-40 5200 Centre Avenue Pittsburgh, PA 15232	**E-mail:** getzenbergrh@msx.upmc.edu	
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EDUCATION AND TRAINING

UNDERGRADUATE:

Dates Attended	*Name and Location of Institution*	*Degree Received and Year*	*Major Subject*
1983 – 1987	Rutgers College, Rutgers University New Brunswick, New Jersey	B.A. w/ High Honors 1987	Microbiology

GRADUATE:

Dates Attended	*Name and Location of Institution*	*Degree Received and Year*	*Major Professor and Discipline*
1987-1992	Johns Hopkins University School of Medicine, Baltimore, Maryland	Ph.D. – 1992	Donald S. Coffey, Ph.D. Biochemistry, Cellular & Molecular Biology

POST-GRADUATE:

Dates Attended	*Name and Location of Institution*	*Name of Program Director and Discipline*
1992-1994	Yale University School of Medicine New Haven, Connecticut	Eric R. Fearon, M.D., Ph.D. Postdoctoral Fellowship Department of Pathology

APPOINTMENTS AND POSITIONS

ACADEMIC:

Years Inclusive	*Name and Location of Institution or Organization*	*Title*
1999 – Present	Department of Urology University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Associate Professor and Director of Urological Research
1999 – Present	Department of Pathology University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Associate Professor
1999 – Present	Department of Pharmacology University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Associate Professor
1994 – 1999	Department of Pathology University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Assistant Professor
1994 – 1999	Department of Surgery University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Assistant Professor
1995 – 1999	Department of Medicine University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Assistant Professor
1995 – 1999	Department of Pharmacology University of Pittsburgh School of Medicine Pittsburgh, Pennsylvania	Assistant Professor
1997 – Present	Prostate and Urologic Cancer Center University of Pittsburgh Cancer Institute	Director of Research and Co-Director
1994 – Present	Prostate and Urologic Cancer Center University of Pittsburgh Cancer Institute	
1995 – Present	Graduate Faculty University of Pittsburgh School of Medicine	
1996 – Present	Cellular and Molecular Pharmacology Graduate Program University of Pittsburgh School of Medicine	Member
1997 – 1998	Cellular and Molecular Pathology Graduate Program University of Pittsburgh School of Medicine	Member, Executive Steering Committee

1998 – Present	Cellular and Molecular Pathology Graduate Program University of Pittsburgh School of Medicine	Associate Director
1999 - Present	UPCI Planning and Budget Committee University of Pittsburgh Cancer Institute	Member
Years Inclusive	*Name and Location of Institution or Organization*	*Title*

MEMBERSHIPS in PROFESSIONAL and SCIENTIFIC SOCIETIES

Organization	*Year*
American Society for Cell Biology	1988 – present
Society for Basic Urologic Research	1992 – present
American Association for Cancer Research	1993 – present
American Urological Association – Affiliate Member	1995 – present
American Association for Clinical Chemistry – Member	2000 - present

HONORS

Title of Award	*Year*
Caspar Nannes Memorial Scholarship Rutgers Club of Washington	1983 – 1987
Henry Rutgers Honor Scholar Rutgers College	1987
Cap and Skull Honor Society, High Skull Rutgers College	1987
High Honors in Microbiology Rutgers College	1987
First Prize, Research, NCI National Meeting on Prostate Cancer, Prouts Neck, Maine	1989
Swebilius Cancer Research Award Yale University School of Medicine	1992 – 1994
American Association for Cancer Research Travel Award Special Conference on Oncogenes and Antioncogenes	1993
Travel Award – Society for Basic Urologic Research Fall Symposium	1993
Shannon Award – National Cancer Institute, National Institutes of Health	1995 – 1997
National Kidney Cancer Association Young Investigator	1996

Honors Convocation – University of Pittsburgh	1997
Society for Basic Urologic Research/Merck Young Investigator Award	1998
Pittsburgh Magazine, "40 under 40" Award	1999
Presenter, American Cancer Society's 41st Science Writers Seminar	1999
Honors Convocation – University of Pittsburgh	2000
Chancellors Research Award – University of Pittsburgh	2000

PUBLICATIONS

1. Refereed articles.

Nath, P., Getzenberg, R.H., Beebe, D., Pallansch, L. and Zelenka, P. c-myc mRNA is Elevated as Differentiating Lens Cells Withdraw From the Cell Cycle. Experimental Cell Research *169*; 215-222, 1988.

Getzenberg, R.H. and Coffey, D.S. Tissue Specificity of the Hormonal Response in Sex Accessory Tissues is Associated with Nuclear Matrix Protein Patterns. Molecular Endocrinology, *4(9)*:1336-1342, 1990.

Getzenberg, R.H., Pienta, K.J. and Coffey, D.S. The Tissue Matrix: Cell Dynamics and Hormone Action. Endocrine Reviews, *11(3)*: 399-417, 1990.

Boyd, J., Pienta, K.J., Getzenberg, R.H., Coffey, D.S. and Barrett, J.C. Preneoplastic Alterations in Nuclear Morphology that Accompany Loss of the Tumor Suppressor Phenotype. Journal of the National Cancer Institute. *83(12)*:862-866, 1991.

Pienta, K.J., Murphy, B.C., Getzenberg, R.H. and Coffey, D.S. The Effect of Extracellular Matrix Interactions on Morphologic Transformation *in vitro*. Biochemical and Biophysical Research Communications, *179(1)*:333-339, 1991.

Getzenberg, R.H., Pienta, K.J., Huang, E.Y.W., Murphy, B.C. and Coffey, D.S. Modifications of the Intermediate Filament and Nuclear Matrix Networks by the Extracellular Matrix. Biochemical and Biophysical Research Communications, *179(1)*:340-344, 1991.

Getzenberg, R.H., Pienta, K.J., Huang, E.Y.W. and Coffey, D.S. Identification of Nuclear Matrix Proteins in the Cancer and Normal Rat Prostate. Cancer Research, *51(24)*:6514-6520, 1991.

Pienta, K.J., Getzenberg, R.H. and Coffey, D.S. Cell Structure and DNA Organization. Critical Reviews in Eukaryotic Gene Expression, *1(4)*:355-385, 1991.

Getzenberg, R.H., Pienta, K.J., Ward, W.S. and Coffey, D.S. Nuclear Structure and the Three-Dimensional Organization of DNA. Journal of Cellular Biochemistry, *47*:289-299, 1991.

Pienta, K.J., Getzenberg, R.H. and Coffey, D.S. Characterization of Nuclear Morphology and Nuclear Matrices in Ageing Human Fibroblasts. Mechanisms of Ageing and Development, *62*:13-24, 1992.

Partin, A.W., Getzenberg, R.H., CarMichael, M.J., Vindivich, D., Yoo, J., Epstein, J.I., and Coffey, D.S. Nuclear Matrix Protein Patterns in Human Benign Prostatic Hyperplasia and Prostate Cancer. Cancer Research, *53(4)*:744-746, 1993.

Getzenberg, R.H. The Nuclear Matrix and the Regulation of Gene Expression: Tissue Specificity. J. Cell. Biochem., *55(1)*:22-31, 1994.

Pierceall, W.E., Cho, K.R., Getzenberg, R.H., Reale, M.A., Hedrick, L., Vogelstein, B., and Fearon, E.R. NIH3T3 Cells Expressing the Deleted in Colorectal Cancer Gene Product Stimulate Neurite Outgrowth in Rat PC12 Pheochromocytoma Cells. J. Cell Biol., *124(6)*:1017-1027, 1994.

Reale, M.A., Hu, G., Zafar, A.I., Getzenberg, R.H., Levine, S.M., and Fearon, E.R. Expression and Alternative Splicing of the Deleted in Colorectal Cancer (DCC) Gene in Normal and Malignant Tissues. Cancer Research, *54(16):*4493-4501, 1994.

Osborn, J.L., Getzenberg, R.H., and Trump, D.L. Spinal Cord Compression in Prostate Cancer. J. Neuro-Onc., *23(2):*135-147, 1995.

Nardozza, T.A., Quigley, M.M., and Getzenberg, R.H. Association of Transcription Factors with the Nuclear Matrix. Journal of Cellular Biochemistry, *61(3):*467-477, 1996.

Getzenberg, R.H., Konety, B.R., Oeler, T.A., Quigley, M.M., Hakam, A., Becich, M.J., and Bahnson, R.R. Bladder Cancer Associated Nuclear Matrix Proteins. Cancer Research, *56:*1690-1694, 1996.

Replogle-Schwab, T.S., Pienta, K.J., and Getzenberg, R.H. The Utilization of Nuclear Matrix Proteins for Cancer Diagnosis. Critical Reviews in Eukaryotic Gene Expression, *6(1&2):*103-113, 1996.

Replogle-Schwab, T.S., Getzenberg, R.H., Donat, T.L., and Pienta, K.J. The Effect of Organ Site of Nuclear Matrix Protein Composition. Journal of Cellular Biochemistry, *62(1),* 132-141, 1996.

Konety, B.R., Getzenberg, R.H., and Bahnson, R.R. Diagnostic and Prognostic Markers in Bladder Cancer. Contemporary Urology, *8(7),* 15-35, 1996.

Konety, B.R., Schwartz, G.G., Acierno, J.S., Becich, M.J., and Getzenberg, R.H. The Role of Vitamin D in Normal Prostatic Growth and Differentiation. Cell Growth and Differentiation, *7,* 1563-1570, 1996.

Getzenberg, R.H., Light, B.W., Lapco, P.E., Konety, B.R., Nangia, A.K., Acierno, J.S., Dhir, R., Shurin, Z., Day, R.S., Trump, D.L., and Johnson, C.S. Vitamin D Inhibition of Prostate Adenocarcinoma Growth and Metastasis in the Dunning Rat Prostate Model System. Urology, *50(6),* 999-1006, 1997.

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Tang, Y., Getzenberg, R.H., Vietmeier, B.N., Sallcup, M.R., Eggert, M., Renkawitz, R., and DeFranco, D.B. The DNA-Binding and ι2 Transactivation Domains of the Rat Glucocorticoid Receptor Constitute a Nuclear Matrix Targeting Signal. Molecular Endocrinology, *12(9),* 1420-1431, 1998.

Konety, B.R., Nangia, A.K., Nguyen, T-S.T., and Getzenberg, R.H. Effect of pre-natal vitamin D (calcitriol) exposure on the growth and development of the prostate and premature death. The Prostate, *41(3),* 181-189, 1999.

Horton, M.J. and Getzenberg, R.H. Rat Seminal Vesicle Secretory Protein SVS-II Binds DNA with a Preference for 5' Regulatory Regions of Secretory Protein Genes: Presence Among Components of the Nuclear Matrix. Journal of Andrology, *20(2)*: 7, 1999.

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Konety, B. R., Leman, E., Vietmeier, B., Arlotti, J. A., Dhir R., and Getzenberg, R. H. In vitro and In vivo Effects of Vitamin D (calcitriol) Administration on the Normal Neonatal and Pre-Pubertal Prostate. Journal of Urology, *164*, 1812-1818, 2000

Konety, B. R., Nguyen, T-S.T., Brenes, G., Sholder, A., Lewis, N., Bastacky, S., Potter, D., and Getzenberg, R. H. Clinical Usefulness of the Novel Marker, BLCA-4, for the Detection of Bladder Cancer. Journal of Urology, *164*: 634-639, 2000.

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Konety, B.R., Nguyen, T-S.T., Dhir, R., Day, R., Stadler, W.M., Becich, M.J., and Getzenberg, R.H. Detection of Bladder Cancer Using a Novel Nuclear Matrix Protein, BLCA-4. Clinical Cancer Research, *6*: 2618-2625, 2000.

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Krill, D., DeFlavia, P., Dhir, R., Luo, J., Leman, E. Becich, M.J., and Getzenberg, R.H. Expression Patterns of Vitamin D Receptor in Human Prostate. Journal of Cellular Biochemistry *82:* 566-572 2001.

Konety, B.R., and Getzenberg, R.H. Urine Based Markers of Urological Malignancy. Journal of Urology, *165*: 600-611, 2001.

Konety, B.R., Somogyi, G., Atan, A., Muindi, J., Chancellor, M.B., Getzenberg, R.H. Evaluation of Intra-Prostatic Metabolism of Vitamin D using a Novel Microdialysis Technique. Journal of Urology, submitted.

Davido, H. T., and Getzenberg, R.H. Utilization of a Urine-Based Assay for BLCA-4 in the Detection of Bladder Cancer. Journal of Clinical Ligand Assay, in press.

Brunagel, G., Vietmeier, B.S., Schoen, R.E., Bauer, A.J., and Getzenberg, R.H. Identification of Specific Nuclear Matrix Proteins in Colon Cancer. Surgical Oncology, in preparation, 2001.

Kulkarni, P., Pirozzi, G., Elashoff, M., Munger, W., Waga, I., Dhir, R., Kakehi, Y., and Getzenberg, R.H. Symptomatic and Asymptomatic Benign Prostatic Hyperplasia: Molecular Differentiation Using Microarrays. Proceedings of the National Academy of Sciences, in press, 2002.

Brunagel, G., Vietmeier, B.N., Bauer, A.J., Schoen, R.E., and Getzenberg, R.H. Identification of Nuclear Matrix Protein Alterations Associated with Human Colon Cancer. Cancer Research, in press, 2002.

Konety, B.R., Somogyi, G., Atan, A., Muindi, J., Chancellor, M.B., and Getzenberg, R.H. Evaluation of Intra-Prostatic Metabolism of 1,25 Dihydroxy vitamin D_3 (Calcitriol) Using a Microdialysis Technique. Urology, in press, 2002.

Leman, E.S., DeMiguel, F., Gao, A.C., and Getzenberg, R.H. Regulation of Androgen and Vitamin D Receptors by 1,25-dihydroxyvitamin D_3 in Human Prostate Epithelial and Stromal Cells. The Prostate, submitted, 2002.

Leman, E.S., and Getzenberg, R.H. Vitamin D Regulation in the Normal and Diseased Prostate. Endocrine Reviews, submitted, 2002.

Masaaki K., Leman E.S., Getzenberg, R.H. and DeFranco, D.B. Common and Distinguishing Features of Steroid Receptor Coactivation by Group 3 LIM Domain Proteins Paxillin and Hic-5/ARA44. American Society for Microbiology, submitted, 2002.

2. Books, Chapters and Reviews.

Getzenberg, R.H., and Coffey, D.S. Tissue Specificity and Cell Death are Associated with Specific Alterations in Nuclear Matrix Proteins, In: Karr, J.P., Tindall, D.J., Coffey, D.S., and Smith, R.G. (eds) Molecular and Cellular Biology of Prostate Cancer, Plenum Press, New York, pg 1-13, 1989.

Pienta, K.J., Murphy, B.C., Getzenberg, R.H., and Coffey, D.S. The Tissue Matrix and the Regulation of Gene Expression in Cancer Cells. Advances in Molecular and Cellular Biology, *7*:131-156, 1993.

Getzenberg, R.H. The Tissue Matrix: Cell Signaling and Hormone Regulation. In: Bittar, E.E. and Bittar, N. (eds) Principles of Medical Biology, JAI Press, Inc., Greenwich, CT, *10B*:643-662, 1997.

Konety, B.R. and Getzenberg, R.H. Novel Therapies for Advanced Prostate Cancer. Seminars in Urologic Oncology, *15(1)*:33-42, 1997.

Horton, M.J. and Getzenberg, R.H. The Role of the Nuclear Matrix in Tissue Specific Gene Expression. In: Getzenberg, R.H. (ed.) Cell Structure and Signalling, JAI Press Inc., Greenwich, CT, 185-206, 1997.

Getzenberg, R.H. Telomerase, Aging and Cancer. AUA News, *2(4)*:10, 1997.

Getzenberg, R.H. Book Review of *Essential Endocrinology*. The Physiologist, in press.

Getzenberg, R.H. Vitamin D and Normal Prostate Growth and Differentiation. Nutrition Report, *15(4)*:25,32, 1997.

Uskokovic, M.R., Trump, D.L., Getzenberg, R.H., and Johnson, C.S. Anticancer Activity of Vitamin D Analogs. In: Holick, M.(ed) Vitamin D Physiology, Molecular Biology, and Chemical Application, Humana Press, Totowa, NJ, in press.

Konety, B.R., Johnson, C.S., Trump, D.L., Getzenberg, R.H. Vitamin D in the Prevention and Treatment of Prostate Cancer. Seminars in Urologic Oncology, *17*:77-84, 1999.

Getzenberg, R.H., Reviewer - Unweaving the Rainbow: Science, Delusion, and the Appetite for Wonder, Author, Richard Dawkins. Oncology Times, 1999.

Getzenberg, R.H. The Nuclear Matrix and Cytoskeleton. The Role of the Nuclear Matrix and Cytoskeleton in Cancer, In: Chung, L. W. K., Isaacs, W. B. and Simons, J. W. (eds) Prostate Cancer: Biology, Genetics, and the New Therapeutics. Humana Press, Totowa, NJ, 2000.

3. Published abstracts.

Hitchens, A.D., Wells, P., Getzenberg, R.H., McDonough, F.E., and Wong, N.P. Modulation of salmonellosis symptoms in weanling rats by a yogurt diet. Fed.Proc., *42*:1188, 1983.

Beebe, D.C. and Getzenberg, R.H. Cell Division During Lens Fiber Differentiation In-vitro. Annual Spring Meeting of the Association for Research in Vision and Ophthalmology, Sarasota, FL. Invest. Ophthalmol. Visual Sci., *27*:215, 1986.

Getzenberg, R.H. and Coffey, D.S. Tissue Specificity and Cell Death are Associated with Specific Alterations in Nuclear Matrix Proteins. National Cancer Institute Meeting on Molecular and Cellular Biology of Prostate Cancer, Prouts Neck, ME, Plenum Press, New York, pg 271, 1989.

Getzenberg, R.H. and Coffey, D.S. Tissue Specificity and Cell Death are Associated with Specific Alterations in Nuclear Matrix Proteins. American Urological Association Annual Meeting, New Orleans, LA. Journal of Urology, *143*:227A, 1990.

Pienta, K.J., Getzenberg, R.H., and Coffey, D.S. Alterations of the Nuclear Matrix in Prostate Cancer. Proceedings American Association for Cancer Research Annual Meeting, Houston, TX. *32*:62, 1991.

Getzenberg, R.H. and Coffey, D.S. Tissue Specific Association of Hormonally Regulated Genes with Tissue Specific Nuclear Matrix Proteins. Society for Basic Urological Research Annual Meeting. Toronto, Ontario, 1991.

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Getzenberg, R.H. and Coffey, D.S. Genes in Sex Accessory Tissues are Differentially Associated with Tissue Specific Nuclear Matrix Proteins. American Urological Association Annual Meeting, Toronto, Ontario, Journal of Urology, *145:*350A, 1991.

Getzenberg, R.H. and Coffey, D.S. Tissue Specific Association of Hormonally Regulated Genes with Tissue Specific Nuclear Matrix Proteins in Sex Accessory Tissues. Proceedings of the Endocrine Society Annual Meeting, Washington, DC: p.400, 1991.

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Replogle-Schwab, T.S., Getzenberg, R.H., Donat, T.L., and Pienta, K.J. The Effect of Organ Site on Nuclear Matrix Protein Composition. Proceedings of the American Association for Cancer Research, *37:*547, 1996.

Konety, B.R., Quigley, M.M., and Getzenberg, R.H. Characterization of a Metastatic Dunning Rat Prostate Tumor Specific Nuclear Matrix Protein (NMP) AM-1. Proceedings of the American Association for Cancer Research, *37:*73, 1996.

Konety, B.R., Quigley, M.M., and Getzenberg, R.H. Identification and Characterization of a Metastatic Rat Prostate Tumor Specific Nuclear Matrix Protein (NMP) AM-1. American Urological Association Annual Meeting, Orlando, FL., 1996.

Butcher, J.L. and Getzenberg, R.H. Association of the Vitamin D Receptor with the Nuclear Matrix. American Urological Association Annual Meeting, Orlando, FL., 1996.

Getzenberg, R.H., Konety, B.R., Becich, M.J., and Schwartz, G.G. Role of Vitamin D in Normal Prostatic Growth and Development. American Urological Association Annual Meeting, Orlando, FL., 1996.

Perdikis, D.A., Reale, M.A., Rieger-Christ, k., Getzenberg, R.H., Fearon, E.R., and Basson, M.D. DCC Gene Expression Inhibits Motility by Modulating the Motile Phenotype in NIH-3T3 Cells. Association for Academic Surgery, 1996.

Getzenberg, R.H., Light, B., Lapco, P., Konety, B., Nangia, A., Trump, D.L., and Johnson, C.S. Vitamin D Inhibition of Prostate Cancer Growth and Metastasis. 7th Prouts Neck Meeting on Prostate Cancer, Prouts Neck, ME, 1996.

Konety, B.R., Nangia, A.K., Becich, M.J., Hrebinko, R.L., and Getzenberg, R.H. Characteristic Nuclear Matrix Protein Alterations in Renal Cell Carcinoma (RCC). American Urological Association Annual Meeting, New Orleans, LA, 1997.

Getzenberg, R.H., Konety, B.R., Nguyen, T.S.T., Vietmeier, B.N., Becich, M.J., Hrebinko, R.L., and Bahnson, R.R. Characterization of Bladder Cancer Associated Nuclear Matrix Proteins. American Urological Association Annual Meeting, New Orleans, LA, 1997.

Getzenberg, R.H., Briggman, J.V., Nguyen, T.S.T., Vietmeier, B.N., and Becich, M.J. Utilization of the Prostate Cancer Specific Nuclear Matrix Protein, D-3 for the Detection of Prostate Cancer. American Urological Association Annual Meeting, New Orleans, LA, 1997.

Light, B. W., Lapco, P. E., Shuring, Z. R., Konety, B. R., Nangia, A. K., Acierno, J. S., Dhir, R., Trump, D. L., Johnson, C. S., and Getzenberg, R. H. *In vivo* inhibition of prostate cancer growth and metastasis by 1,25-hydroxycholecalciferol in the MatLyLu Dunning rat prostate model. Proceedings of the American Association for Cancer Research, 1997.

Lapco. P. E., Light, B. W., Konety, B. R., Nangia, A. K., Trump, D. L., Johnson, C. S., and Getzenberg, R. H. In vitro effects of 1,25-dihydroxycholecalciferol on Dunning prostate cancer cells. Proceedings of the American Association for Cancer Research, 1997.

Konety, B. R., Schwartz, G. G., Becich, M. J., and Getzenberg, R. H. Role of Vitamin D in Normal Prostatic Growth and Development. Tenth Workshop on Vitamin D., Strasbourg, France, 1997.

Getzenberg, R. H., Light, B. W., Lapco, P. E., Konety, B. R., Nangia, A. K., Acierno, J. S., Dhir, R., Shurin, Z., Day, Roger S., Trump, D. L., and Johnson, C. S. Vitamin D Inhibition of Prostate Cancer Growth and Metastasis *in vivo* and *in vitro*. Tenth Workshop on Vitamin D., Strasbourg, France, 1997.

Johnson, C. S., McElwain, M. C., Light, B. W., Yu, W-D., Trump, D. L., and Getzenberg, R. H. Anti-Proliferative Effects of Vitamin D and its Analogs in Rodent Tumor Models. Tenth Workshop on Vitamin D., Strasbourg, France, 1997.

Trump, D. L., Smith, D. C., Muindi, J., Brufsky, A., Freeman, C., Wilson, J., Getzenberg, R. H., and Johnson, C. S. 1,25 Dihydroxycholecalciferol (1,25 1)3): Preclinical Rationale and Status of Phase I Clinical Trials of Subcutaneous 1,25 D3 - A New Chemotherapeutic Agent. Tenth Workshop on Vitamin D., Strasbourg, France, 1997.

Johnson, C. S., McElwain, M. S., Yu, W-D., Modzelewski, R. A., Light, B. W., Trump, D. L., and Getzenberg, R. H. Vitamin D: A Potential Therapeutic Agent for Solid Tumors. Greece, 1997.

Getzenberg, R. H., Konety, B. R., Nguyen, T-S. T., Vietmeier, B. N., Becich, M. J. and Bahnson, R.R. Characterization of Bladder Cancer Associated Nuclear Matrix Proteins. 2nd World Congress on Urological Research, Pacific Grove, CA, 1997.

Horton, M. J. and Getzenberg, R. H. DNA-Binding Activity of the Rat Seminal Vesicle Secretory Protein SVS-II. Annual Meeting of The American Society for Cell Biology, Washington, DC. 1997.

Getzenberg, R. H., Konety, B. R., Nguyen, T-S. T., Vietmeier, B. N., Becich, M. J. and Bahnson, R.R. Characterization of Bladder Cancer Associated Nuclear Matrix Proteins. AACR Conference on Innovative Approaches to the Prevention, Diagnosis and Therapy of Cancer, Maui, HI, 1998.

Getzenberg, R. H., Konety, B. R., Nguyen, T-S. T., Vietmeier, B. N., Becich, M. J. and Bahnson, R. R. Characterization of the Bladder Cancer Specific Nuclear Matrix Protein, BLCA-4. Proceedings of the American Association for Cancer Research, *39:* 467, 1998.

Konety, B. R., Nangia, A. K., Dhir, R., Becich, M. J., and Getzenberg, R. H. The Effect of Vitamin D on the Developing Prostate. Proceedings of the American Association for Cancer Research, *39:105,* 1998.

Nangia, A. K., Butcher, J., Konety, B. R., Vietmeier, B. N., and Getzenberg, R. H. Association of Vitamin D Receptors with the Nuclear Matrix of Human and Rat Genitourinary Tissues. American Urological Association Annual Meeting, San Diego, CA, *159:1,* 1998.

Konety, B. R., Nangia, A. K., Dhir, R., Becich, M. J., and Getzenberg, R. H. The Effect of Pre-Natal Vitamin D Exposure on Subsequent Prostatic Development. American Urological Association Annual Meeting, San Diego, CA, *159:* 107, 1998.

Getzenberg, R.H., Nguyen, T-S.T., Vietmeier, B.N., Bastacky, S., Konety, B.R. Utilization of the Bladder Cancer Specific Nuclear Matrix Protein, BLCA-4, for the Detection of Bladder Cancer. 8th Annual Society for Basic Urologic Research Fall Symposium (SBUR), Prouts Neck, ME, 1998.

Konety, B.R., Nangia, A.K., Thomas, A., Dhir, R., Becich, M.J., and Getzenberg, R.H. The Effect of Vitamin D on the Developing Prostate. 8th Annual Society for Basic Urologic Research Fall Symposium (SBUR), Prouts Neck, ME, 1998.

Vietmeier, B.N., Stella, A., Liu, B., and Getzenberg, R.H. Characterization of the of the Rat Prostate Cancer Nuclear Matrix Protein, D-2. Proceeding of the American Association for Cancer Research, 1999.

Arlotti, J.A., Cimino, T.S., Nyguyen, T.S., Thomas, A., Dhir, R., Jaynes, J.M., Caldwell, A.L., and Getzenberg, R.H. Efficacy of a Synthetic Lytic Peptide in the Treatment of Prostate Cancer. Proceeding of the American Association for Cancer Research, 1999.

Nguyen, T-S.T., Vietmeier, B.N., Bastacky, S., Konety, B.R., and Getzenberg, R.H. Utilization of the Bladder Cancer Specific Nuclear Matrix Protein, BLCA-4 for the Detection of Bladder Cancer. Proceeding of the American Association for Cancer Research, 1999.

Konety, B.R., Pirtskalashvili, G., Hershberger, P., Johnson, C.S., Getzenberg, R.H. Vitamin D induced apoptosis of bladder tumor cells in vitro. Proceeding of the American Association for Cancer Research, 1999.

Konety, B.R., Nguyen, T-S.T., Day, R.S., Sholder, A., Brenes, G., Bastacky, S., Getzenberg, R.H. Evaluation of urinary nuclear matrix protein (BLCA-4) levels in patients with spinal cord injury. Proceeding of the American Association for Cancer Research, 1999.

Konety, B., Pirtskalashvili, G., Hershberger, P., Johnson, C., Getzenberg, R. Vitamin D induced apoptosis of bladder tumor cells in vitro. American Urological Association Meeting, Dallas, Texas, 1999.

Nguyen, T-S.T., Vietmeier, B.N., Bastacky, S., Konety, B.R., Getzenberg, R. Utilization of the bladder cancer specific nuclear matrix protein, BLCA-4, for the detection of bladder cancer. American Urological Association Meeting, Dallas, Texas, 1999.

Nguyen, T-S.T., Vietmeier, B.N., Bastacky, S., Konety, B.R., Getzenberg, R. Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer. American Urological Association Meeting,

Atlanta, Georgia, 2000.

Nguyen, T-S.T., Vietmeier, B.N., Bastacky, S., Konety, B.R., Getzenberg, R. Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer. Proceeding of the American Association for Cancer Research, San Francisco, CA, 2000.

Arlotti, J. A., Cimino, T. S., Nguyen, T-S.T., Dhir, R., Thomas, A., Jaynes, J. M., Caldwell, A. L., and Getzenberg, R. H. Efficacy of a Synthetic Lytic Peptide in the Treatment of Prostate Cancer. American Urological Association Meeting, Atlanta, Georgia, 2000.

Konety, B. R., Nguyen, T-S.T., Brenes, G., Sholder, A., Lewis, N., Potter, D., Bastacky, S., and Getzenberg, R. H. Utility of the Urine Based Biomarkers BLCA-4 in the Detection of Bladder Cancer in Individuals with Spinal Cord Injury (SCI). American Urological Association Meeting, Atlanta, Georgia, 2000.

Konety, B. R., Nguyen, T-S.T., Lavelle, J. P., Zeidel, M. L., and Getzenberg, R. H. Expression of BLCA-4, a Nuclear Matrix Protein (NMP) Marker in a Carcinogen Induced Model of Bladder Cancer. American Urological Association Meeting, Atlanta, Georgia, 2000.

Konety, B. R., Lavelle, J. P., Pirtskalaishvili, G., Calleary, J. G., Meyers, S. A., Ramage, R., Dhir, R., Zeidel, M. L., and Getzenberg, R. H. Evaluation of Vitamin D in the Prevention and Treatment of Bladder Cancer. American Urological Association Meeting, Atlanta, Georgia, 2000.

Konety, B. R., Leman, E., Vietmeier, B. N., Arlotti, J., Dhir, R., and Getzenberg, R. H. In Vitro and In Vivo Effects of Vitamin D Administration on the Normal Neonatal and Pre-Pubertal Prostate. American Urological Association Meeting, Atlanta, Georgia, 2000

Konety, B. R., Somogyi, G., Atan, A., Muindi, J., Chancellor, M. B., and Getzenberg, R. H. Evaluation of Intra-Prostatic Metabolism of Vitamin D Using a Novel Microdialysis-Technique. American Urological Association Meeting, Atlanta, Georgia, 2000

Leman, E.S., Arlotti, J.A., Greenberg, N., and Getzenberg, R.H. Characterization of the Nuclear Matrix Proteins During the Development of Prostate Cancer in a Mouse Model. Society for Basic Urologic Research Fall Symposium, Ft. Myers, Florida, 2000

Nguyen, T-S.T., Konety, B.R., Erdos, G., and Getzenberg, R.H. Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer. Society for Basic Urologic Research Fall Symposium, Ft. Myers, Florida, 2000

Vietmeier, B.N., Stella, A., Liu, B. and Getzenberg, R.H. Characterization of the Rat Prostate Cancer Nuclear Matrix Protein, D-2. Society for Basic Urologic Research Fall Symposium, Ft. Myers, Florida, 2000

Arlotti, J.A., Konety, B.R., Greenberg, N.M., Bastacky, S.I., Leman, E.S., and Getzenberg. Chemopreventive Efficacy of Vitamin D in a Mouse Model. Society for Basic Urologic Research Fall Symposium, Ft. Myers, Florida, 2000

Davido, H.T., Konety, B.R., and Getzenberg, R.H. Bladder Cancer and Spinal Cord Injury. Society for Basic Urologic Research Fall Symposium, Ft. Myers, Florida, 2000

Whalen, J.D., Mi, Z., Mai, J., Robbins, P.D., and Getzenberg, R.H. Protein Transduction: A New

Strategy in the Treatment of Prostate Cancer Metastasis To Bone. Society for Basic Urologic Research Fall Symposium, Ft. Myers, Florida, 2000

Nguyen, T-S.T., Davido, T., Konety, B. R., and Getzenberg, R.H. Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer. American Association for Cancer Research, New Orleans, LA, 2001

Kakehi, Y., Kulkarni, P., Dhir, R., Pirozzi G., Munger, W., and Getzenberg, R.H. Molecular Differentiation of Histologic and Symptomatic BPH. American Urological Association Meeting, Anaheim, CA, 2001

Nguyen, T-S.T., Davido, T., Konety, B. R., and Getzenberg, R.H. Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer. American Urological Association Meeting, Anaheim, CA, 2001

Bruenagel, G., Vietmeier, B.S., Schoen, R.E., Bauer, A.J., and Getzenberg, R.H. Identification of Specific Nuclear Matrix Proteins in Colon Cancer. American College of Surgeons, 2001

Nguyen, T-S.T., Davido, T., Konety, B. R., and Getzenberg, R.H. Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer. European Congress of Clinical Chemistry and Laboratory Medicine, Prague, Czech Republic, 2001

Bruenagel, G., Bauer, T.A., Schoen, R.E., and Getzenberg, R.H. Identification of Specific Nuclear Matrix Protein Alterations in Human Colon Cancer. Federation of American Societies for Experimental Biology (FASEB) Summer Research Conference, Saxtons River, Vermont, 2001

Leman, E.S., Arlotti, J.A., Greenberg, N., and Getzenberg, R.H. Characterization of the Nuclear Matrix Proteins During the Development of Prostate Cancer in a Mouse Model. Federation of American Societies for Experimental Biology (FASEB) Summer Research Conference, Saxtons River, Vermont, 2001

Nguyen, T-S.T., Konety, B.R., Myers, J.M., and Getzenberg, R.H. A Highly Novel Specific and Sensitive Urine-Based Assay for the Detection of Bladder Cancer. XVIIth Congress of the European Association of Urology (EAU) Scientific Meeting. Birmingham, England, 2002.

Shah, U.S., Dhir, R. and Getzenberg, R.H. Characterization of a Novel Protein, JM27, in Prostate Cancer Cell Lines. American Association for Cancer Research, Naples, FL, 2001.

Leman, E.S., DeMiguel, F., Gao, A.C. and Getzenberg, R.H. Regulation of the Androgen and Vitamin D Receptors by 1,25-dihydroxyvitamin D_3 in Human Prostate Epithelial Cells. American Association for Cancer Research, Naples, FL, 2001.

Prakash, K., Pirozzi, G., Elashoff, M., Munger, W., Waga, I., Kanagawa, Y., Dhir, R., Kakehi, Y. and Getzenberg, R.H. Differentiation Symptomatic and Asymptomatic BPH: JM-27. American Association for Cancer Research, Orlando, FL, 2002.

Prakash, K., Pirozzi, G., Elashoff, M., Munger, W., Waga, I., Kanagawa, Y., Dhir, R., Kakehi, Y. and Getzenberg, R.H. Genetic Similarity of BPH from Individuals with Symptoms and Those with Prostate Cancer. American Association for Cancer Research, Orlando, FL, 2002.

Nguyen, T-S.T., Konety, B.R., Myers, J.M., and Getzenberg, R.H. A Novel Highly Specific and

Sensitive Urine-Based Assay for the Detection of Bladder Cancer. American Association for Clinical Chemistry, La Jolla, CA, 2002.

Leman, E.S., DeMiguel, F., Gao, A.C. and Getzenberg, R.H. Regulation of the Androgen and Vitamin D Receptors by 1,25-dihydroxyvitamin D_3 in Human Prostate Epithelial Cells. American Association for Cancer Research, San Francisco, CA, 2002.

Leman, E.S., Arlotti, J.A., Greenberg, N., and Getzenberg, R.H. Characterization of the Nuclear Matrix Proteins During the Development of Prostate Cancer in a Mouse Model. American Association for Cancer Research, San Francisco, CA, 2002.

Shah, U.S. and Getzenberg, R.H. Identification of a Potential Growth Regulatory Gene Demonstrating a "Field Effect" In Prostate Cancer. American Association for Cancer Research, San Francisco, CA, 2002

Bruenagel, G., Bauer, T.A., Schoen, R.E., and Getzenberg, R.H. Identification of Specific Nuclear Matrix Protein Alterations in Human Colon Cancer and Polyps. Fifth EDRN Steering Committee Meeting, Houston, Texas, 2002.

Nguyen, T-S.T., Konety, B.R., Myers, J.M., and Getzenberg, R.H. A Novel Highly Specific and Sensitive Urine-Based Assay for the Detection of Bladder Cancer. XVIIth Congress of the European Association of Urology, Birmingham, England, 2002.

Björnsson, Björn L., Sylvester, R., Getzenberg, R.H., Oosterlinck, Willem and Goebell, Peter, J. Comprehensive Analysis of Urine-Based Markers for Bladder Cancer – The Proposed Multicenter Urothelial Neoplasia Detection (MUND) Study. 2nd International NCI-EORTC Meeting on Cancer Diagnostics, Cambridge, Maryland, 2002.

Getzenberg, R.H., Davido, T., Konety B.R., Van Le, T-S.T. A Highly Specific and Senstitive Urine-Based Assay for the Detection of Bladder Cancer. Oak Ridge Conference – Cancer Detection and Monitoring: The Next Generation of Diagnostic Tools. La Jolla, California, 2002

PROFESSIONAL ACTIVITIES

TEACHING:

1994	"The Role of Nuclear Structure in Gene Regulation and Cancer" Medical Oncology Grand Rounds, University of Pittsburgh Medical Center Pittsburgh, PA
1994	"The Role of the Nuclear Matrix in Prostate Cancer" Urology Grand Rounds, University of Pittsburgh Medical Center, Pittsburgh, PA
1994–Present	Organized bi-monthly research conference for investigators, fellows and students with interests in prostate and GU cancers.
1994–Present	Cancer Research and the Pittsburgh Cancer Institute Presented a weekly orientation for local High School students sponsored by the LHAS.
1994- 1995	Sponsored Directed Research (Course # Bioscience 1903) for undergraduate Jeff Butcher entitled, "Examination of Vitamin D Receptors on the Nuclear Matrix"
1995	Sponsored Directed Research (Course # Bioscience 1903) for undergraduate Tisha Nardozza entitled, "Association of Transcription Factors with the Nuclear Matrix"
1995	"The Role of the Nuclear Matrix in Gene Regulation and Cancer" Department of Pharmacology Seminar, University of Pittsburgh Medical Center Pittsburgh, PA
1995	"The Role of the Nuclear Matrix in Gene Regulation and Cancer" Human Genetics Seminar - HUGEN 2025, University of Pittsburgh Pittsburgh, PA
1995	Pittsburgh Cancer Institute Orientation
1995	Lectured in Department of Pharmacology Graduate Course, *Cancer Pharmacology*
1995	Facilitator for Medical Student course *Cancer Pharmacology*
1995	Comprehensive Examination Committee, Edwina C. Lerner Department of Pharmacology
1995- 1996	Training of Dr. Badrinath R. Konety, Urology Resident Laboratory Research
1995–Present	Thesis Committee, Yuting Tang Department of Biology - Donald DeFranco, Thesis Advisor
1996	Pharmacology Course Problem Based Learning Session Leader

1996	Lectured in Department of Pharmacology Graduate Course, *Cancer Pharmacology*
1996	Lectured in "From Bench to Bedside - Frontiers in Cancer Research University of Chicago
1996	Integrated Life Sciences - Neoplastic Disease Course (2/96-3/96)
1996	Comprehensive Examination Committee, Marni Brisson Department of Pharmacology
1996	Training of Dr. Ajay K. Nangia, Urology Resident Laboratory Research
1996	"Recent Advances in Prostate and Bladder Cancer" Urology Grand Rounds, University of Pittsburgh Medical Center, Pittsburgh, PA
1996	Laboratory Research Rotation, Lei Zheng, Department of Pathology, Graduate Student
1996	Training of Amy Abdulovic, High School Student Intern
1997	Lectured in Graduate Biochemistry Course, West Virginia University, Department of Biochemistry, "Nuclear Matrix and Regulation"
1997	Pharmacology Course Problem Based Learning Session Leader
1997	UPCI, Biologic Therapy Program, Biologic Therapy and Transplantation Research Colloquia, "Novel Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D"
1997	Cancer Research, National Defense University, Industrial College of the Armed Forces, University of Pittsburgh Cancer Institute
1997	Faculty, 1997 American Urological Association Annual Meeting, "Understanding Molecular Techniques and Their Applications to Urology", New Orleans, LA
1997	Facilitator for Medical Student *Pharmacology Conference on Host Defenses*
1997	Lectured in Department of Pharmacology Graduate Course, *Cancer Pharmacology*
1997	Hematology/BMT Research Seminar. "Novel Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D"
1997	Judge - 8th Annual Department of Pathology Research Presentations
1997	Cancer and Cancer Research, Visiting Nurses from Japan, University of Pittsburgh Cancer Institute
1997	Presented to UPCI Council Members
1997	"The Nuclear Matrix and Cancer" Medical Oncology Grand Rounds, University of Pittsburgh School of Medicine Pittsburgh, PA

1997	"Cancer Associated Nuclear Matrix Proteins" Pathology Research Seminar, University of Pittsburgh School of Medicine, Pittsburgh, PA
1997-1999	Thesis Committee, Jimin Liu Department of Biology - Donald DeFranco, Thesis Advisor
1997	Cancer and Cancer Research, Nursing Students, University of Pittsburgh Cancer Institute
1997-1998	Thesis Committee, Jen-Tzer Gao Department of Pathology - Michael J. Becich, Thesis Advisor
1997–1998	Supervised Undergraduate Research Project of Kyle Fisher
1998	Pharmacology Course Problem Based Learning Session Leader
1998	Facilitator for Medical Student *Pharmacology Conference on Host Defenses*
1998-Present	Prostate Cancer and Cancer Metastasis Lectures of School of Medicine Graduate Course, "Cancer Biology", University of Pittsburgh School of Medicine
1998	Lectures of School of Medicine Course, "Tissue Structure, Growth and Function". University of Pittsburgh School of Medicine
1998	Cancer Research, National Defense University, Industrial College of the Armed Forces, University of Pittsburgh Cancer Institute
1998	Faculty, 1998 American Urological Association Annual Meeting, "Understanding Molecular Techniques and Their Applications to Urology", San Diego, CA
1998-2000	Preceptor for Dr. Badrinath R. Konety, American Foundation for Urologic Disease and Foundation for Strategic Bladder Research Scholar
1998-Present	Thesis Committee, Jennifer Guerrero Department of Biology - Donald DeFranco, Thesis Advisor
1998-2000	Thesis Committee, Mark Whitmore Department of Pharmacology - Leaf Huang, Thesis Advisor
1998	Summer Internship, Amy Abdulovic Grove City College
1998	Comprehensive Examination Committee, Yadi Tan Department of Pharmacology
1998	Research Rotation, M.D., Ph.D. Program Jared Muenzer
1998	Lectured in the Medicine, Ethics and Society Course, School of Medicine
1998	Presentation on Medical Ethics to M.D., Ph.D. Students, University of Pittsburgh School of Medicine

1998-Present	Co-Director and Lecturer Neoplasia and Neoplastic Diseases Course, Medical Students, University of Pittsburgh School of Medicine
1998-1999	Thesis Committee, Michael Gray Molecular Genetics and Biochemistry – Bo Liu, Thesis Advisor
1998-Present	Faculty Advisor, Interdisciplinary Graduate Program Eddy Leman
1999	"New Marker to Detect Bladder Cancer". Healthsouth Harmarville Rehabilitation Hospital, Rehabilitation Mini-Grand Rounds, Harmarville, PA.
1999	Lectured on Prostate Biology in "Tissue Structure, Growth and Function". University of Pittsburgh School of Medicine.
1999	Pharmacology Course Problem Based Learning Session Leader
1999	Training of Kate Dougherty – High School Intern
1999	Research Rotation, Interdisciplinary Graduate Program – Matthew Wilson
1999	Lectured in the Medicine Ethics and Society Course, School of Medicine
1999	Lectured in the Foundations of Biomedical Science, School of Medicine
1999	"The Role of the Nuclear Matrix in Gene Regulation and Cancer" Pharmacology Research Seminar, University of Pittsburgh School of Medicine, Pittsburgh, PA
1999	Research Rotation, Interdisciplinary Graduate Program – Andrew Lepisto
1999	"Cancer and Cancer Research" Grove City College, Grove City, PA
2000	Lectured on Prostate Biology in "Tissue Structure, Growth and Function". University of Pittsburgh School of Medicine.
2000	"Current Advances in Bladder Cancer" Armstrong County Memorial Hospital – Tumor Board Kittanning, PA
2000	Summer Internship, Amy Abdulovic Grove City College
2000	Summer Internship, Roger Bartollota
2000	Course Director/Integrated Life Sciences Course/Neoplasia and Neoplastic Disease – University of Pittsburgh

2000	Pathobiology Course – Lecturer "Nuclear Controls and Transcription Regulation in Prostate Cancer"
2000-2001	Training of Tracy Davido, Medical Student IV Laboratory Research
2000-2002	Training of Janey Whalen, Ph.D. Postdoctoral Fellow
2000	Lectured in the Medicine Ethics and Society Course, School of Medicine
2000	Research Rotation, Jared Muenzer, Medical Student IV
2000-2002	Gisela Brüenagel, M.D. Postdoctoral Fellow-Feodor Lynen Fellowship Award
2000-2001	Research Rotation, Interdisciplinary Graduate Program – Lana Hanford
2000	Lectured in the Foundations of Biomedical Science, School of Medicine
2000	Lectured in the Medicine Ethics and Society Course, School of Medicine
2001	Course Director/Integrated Life Sciences Course/Neoplasia and Neoplastic Disease University of Pittsburgh
2001	Lectured on Prostate Biology in "Tissue Structure, Growth and Function" University of Pittsburgh School of Medicine
2001-Present	Interdisciplinary Graduate Program – Julie Myers
2001	Thesis Committee, Department of Pathology – Lei Zheng, Michael J. Becich, Thesis Advisor
1999-Present	Interdisciplinary Graduate Program – Eddy Leman
2001	Summer Internship, Pittsburgh Tissue Engineering Initiative, Inc. – Michael Madigan
2001	Summer Undergraduate Research Program – Elizabeth Pino
2001	Summer Internship, Amy Abdulovic / Grove City College
2001-Present	Training of Uzma Shah, Ph.D. Postdoctoral Fellow
2001	Cancer Biology and Therapeutics Course - Lecturer "Biology of Transformation: Invasion and Metastasis" Departments of Pathology & Pharmacology – University of Pittsburgh
2001	Pathobiology Course – Lecturer "Nuclear Controls and Transcription Regulation in Prostate Cancer"

2001	Lectured in the Foundations of Biomedical Science, School of Medicine
2001	Lectured in Human Genetics Seminar, School of Medicine "Novel Approaches to Urologic Diseases: Cancer and BPH"
2002	Thesis Committee, Department of Pathology – Lei Zheng, Michael J. Becich, Thesis Advisor
2002	Lectured in Integrated Life Sciences Course/Neoplasia and Neoplastic Disease – University of Pittsburgh
2002	Summer Internship – Kristin Stolarczyk / Penn State University
2001-2002	Undergraduate Research Program – Marie Aquilano

RESEARCH:

1. Grant Support
Active

Grant Number (Funded)	Grant Title	Role in Project & Percentage of Effort	Years Inclusive	Source
1RO1 DK52697	Effects of Vitamin D on Human Prostate Growth	Principal Investigator 24.7%	1997-2002	NIH
1RO1 CA82522-01A1	Characterization of the Bladder Cancer NMP, BLCA-4	Principal Investigator 25%	2000-2005	NIH
5P 30 CA47904-13	Prostate and Urologic Cancer Program-UPCI Cancer Center Core Grant	Principal Investigator 5%	1999-2004	NIH
1 K12 DK02656-01 1 T32 DK07774-01	Physicians and Scientist Training Program in Urologic Research	Co-Investigator 5%	1999-2004	NIH
N0I-CN-75018	A Phase II Clinical Trial of Anti-Androgen and 5-alpha Reductase Inhibitors in Patients With Prostate Cancer. Administration in the Period Prior to Radical Prostatectomy (Presurgical Period). Modulation of Surrogate Endpoint Biomarkers (Seb)	Co-Investigator 0%	1996-2001 (extended)	NIH
	Sponsored Research Agreement	Principal Investigator 10%	2002-2003	Tessera Diagnostics, Inc.
	Sponsored Research Agreement	Principal Investigator 0%	1999-2002	Eichrom Technologies, Inc.
1 R13 CA091916	FASEB Conference: Nuclear Structure and Cancer	Conference Co-Chair 0%	2001-2001	NIH
1 P01 HD39768-01	Collaborative Urologic Research In Spinal Cord Injury- Project 3-Biomarkers of Bladder Cancer in SCI Individuals	Principal Investigator 12.75%	2001-2006	NIH
DAMD3058093	A Novel Approach in Prostate In Prostate Cancer Therapy	Co-Investigator 10%	2001-2004	DOD

N01-CO-17016-32	Development of an *in-vivo* Sensing Technology for the Development of Biomolecular Sensors	Co-Investigator 10%	2001-2004	NIH

Previous

Grant Number (Funded)	Grant Title	Role in Project & Percentage of Effort	Years Inclusive	Source
1R55 CA/OD65463	Shannon Award	Principal Investigator	1995-1997	NIH
	Evaluation of Nuclear Matrix Protein Markers in Renal Cell Carcinoma	Principal Investigator	1996-1997	National Kidney Foundation of W. Penn.
	Induction of an Immune Response to Normal Prostate Antigens as an Immunotherapeutic Strategy for Prostate Cancer	Co-Investigator	1996-1997	CaP CURE
	Bladder Cancer Associated Nuclear Matrix Alterations	Principal Investigator	1996-1997	Comp. Medical Research Fund
	The Clinical Utility of Renal Cell Carcinoma Associated Nuclear Matrix Proteins	Principal Investigator	1996-1997	National Kidney Cancer Assoc.
	Sponsored Research Agreement	Principal Investigator	1996-1997	Matritech
	Demeter Bio Technologies Ltd.	Principal Investigator	1997-2000	Demeter
1RO3 HD35878	Spinal Cord Injury and Bladder Cancer Detection	Principal Investigator 10%	1998-2000	NIH
	The Study of LY353381 In Prostate Cancer	Principal Investigator	1998-2000	Lilly & Co.
	Role of Extracellular Matrix And Nuclear Structure Interactions in Gene Expression And Breast Cancer: Use of a 3D Culture Model of Human Mammary Tumorigenesis	Consultant	1997-2000	DOD
	Chemoprevention of Urinary Bladder Cancer by NSAIDS	Consultant	2000- 2001	University of Alabama at Birmingham
1R01 CA65463	Prostate Cancer Associated Nuclear Matrix Alterations	Principal Investigator 25%	1996-2001	NIH

	Sponsored Research Agreement	Principal Investigator	1999-2002	TAP Pharm.
	Sponsored Research Agreement	Principal Investigator	1999-2002	GeneLogic

Pending

Grant Number (Funded)	Grant Title	Role in Project & Percentage of Effort	Years Inclusive	Source
R01-CA65463	Prostate Cancer Associated Nuclear Matrix Protein D-2	Principal Investigator 30%	2002-2007	NIH
NCI-1CFAMB 10042	NMPs as Early Markers of Of Colorectal Cancer	Principal Investigator 5%	2001-2003	NIH
R01-CA96105-01	Specific Biomarkers in Bladder Cancer Prevention	Principal Investigator 25%	2002-2005	NIH
NIH-R13CA/DK97015	Prouts Neck Prostate Cancer Meetings	Principal Investigator 0%	2002-2006	NIH
NIH-R01 52697-06	Vitamin D Effects on Human Prostate Growth	Principal Investigator 25%	2002-2007	NIH
NIH-R01	Characterization of the Colon NMP, CC-2	Principal Investigator 15%	2002-2007	NIH
NIH-R01 DK063022	JM-27, A Potential Regulator of Symptomatic BPH	Principal Investigator 25%	2002-2007	NIH
NIH-RFA	MTOPS Biomarker Unit at the University of Pittsburgh	Principal Investigator 25%	2002-2005	NIH

Patent Applications

Partin, A.W., Getzenberg, R.H., and Coffey, D.S., "Nuclear Matrix Proteins", U.S. Serial No. 08/015,624, 1993 (Awarded 9/97).

Getzenberg, R.H., "Nuclear Matrix Proteins, Polynucelotide Sequences Encoding Them, and Their Use", U.S. Serial No. 09/418,839, 1999 (Pending).

Getzenberg, R.H. and Bahnson, R.R., "Bladder Cancer Nuclear Matrix Proteins", 1995. U.S. Patent Number 5,866.535 (Awarded 2/99).

Getzenberg, R.H., "Renal Nuclear Matrix Proteins and Their Use", 1997. U.S. Patent Number 6,232,443 (Awarded 5/01).

Munger, W.E., Kulkarni, P., and Getzenberg, R.H., GeneLogic – "Identification of cDNAs Associated with Benign Prostatic Hyperplasia", 2000 (Pending).

Getzenberg, R.H., Bauer, A.J., Schoen, R.E., Bruenagel, G., "Colonic Nuclear Proteins, Polynucleotide Sequences, Encodin Them and Their Use", Supported by NCI – Grant No. U01 CA84968, 2001 (Pending)

2. Seminars and invited lectureships related to your research

1990 "Tissue Specificity of the Nuclear Matrix in Hormone Action"
Annual Meeting of the American Society for Cell Biology, San Diego, CA.

1991 "Interaction of Tissue Specific Genes with Tissue Specific Nuclear Matrix Proteins in Rat Sex Accessory Tissues"
Annual Meeting of the American Society for Cell Biology, Boston, MA.

1992 "Nuclear Matrix Alterations Associated with Prostate Cancer in the Dunning Model"
American Urological Association Annual Meeting, Washington, DC.

1992 "Characterization of the Tissue Matrix Components of the Normal Prostate and Benign Prostatic Hyperplasia in the Beagle"
American Urological Association Annual Meeting, Washington, DC.

1992 "Tissue Specific DNA Organization and the Nuclear Matrix: Normal and Cancer Cells"
National Institutes of Health, Bethesda, MD.

1993 Gordon Conference on Biological Structure and Gene Expression
Volterra, Italy

1994 FASEB Conference – Molecular Genetic Basis of Cell and Tissue Structure and Function
Copper Mountain, CO

1995 "Characterization of Prostate Cancer Associated Nuclear Matrix Alterations"
American Urological Association Annual Meeting, Las Vegas, NV

1995 "The Role of the Nuclear Matrix in Prostate Cancer"
Society for Basic Urologic Research – 5th Annual Fall Symposium, Chapel Hill, NC

1995 "Recent Studies in Cancer Associated NMPs: Rat Prostate and Human Bladder"
Matritech, Inc., Cambridge, MA

1996 "Prostate and Bladder Cancer Associated Nuclear Matrix Proteins"
Hematology/Oncology Research Seminar, University of Michigan School of Medicine

1996 Prostate Cancer Prevention Workshop: Investigational Approaches and Opportunities for Preventing Prostate Cancer, National Cancer Institute, Annapolis, MD.

1996 "Characterization of Prostate and Bladder Cancer Associated Nuclear Matrix Proteins" Nuclear Structure-Gene Expression Interrelationships, Cambridge Symposia, Bolton Valley, VT

1996 "Prostate and Bladder Cancer Associated Nuclear Matrix Proteins"
The University of Chicago, Chicago, IL

1996 "Nuclear Matrix Organization" Faculty, American Urological Association 1996 Research Conference, "Advances in Cell Biology", Houston, TX.

1996 "The Nuclear Matrix and its Role in Cancer"
Visiting Speakers in Cancer, Case Western Reserve University, Cleveland, OH

1996 "Novel Approaches to Prostate Cancer: Nuclear Matrix and Vitamin D"
Prostate Cancer Program, Eli Lilly & Co., Indianapolis, IN

1996 "The Nuclear Matrix and Cancer"
Behring Diagnostics Inc., San Jose, CA

1997 "The Nuclear Matrix and its Role in Cancer"
Department of Biochemistry, West Virginia University

1997 "Novel Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D"
GU Oncology Conference, University of Michigan, Ann Arbor, MI

1997 "Nuclear Protein Matrix"
National Kidney Cancer Association Scientific Conference, Short Hills, NJ

1997 International Workshop on Diagnostic and Prognostic Markers in Bladder Cancer, Barcelona, Spain

1997 Judge-Third Annual Oakland Scientific Conference, Pittsburgh, PA

1997 "The Nuclear Matrix and Cancer"
Bard Diagnostic Sciences, Inc., Redmond, WA

1997 Animal Models of Prostate Cancer – International Commission on Urological Diseases
Purdue University, West Lafayette, IN

1998 "Nuclear Matrix Proteins"
Bladder Cancer: New Concepts in Biology and Therapy, Sarasota, FL

1998 "Analysis of Demeter Peptide D2A21"
Pacific West Cancer Foundation, Maui, HI

1998 "Cancer and Cancer Research"
Seton Hill College, Greensburg, PA

1998 "The Nuclear Matrix and Cancer"
Ortho-Clinical Diagnostics, Raritan, NJ

1998 "Cancer Associated Nuclear Matrix Proteins"
Keystone Symposia, The Nuclear Matrix: Involvement in Genomic Organization, Function and Cellular Regulation, Copper Mountain, CO

1998 "The Nuclear Matrix and Cancer"
Bristol-Myers Squibb Oncology, Princeton, NJ

1998 Kidney Cancer Futures Forum
National Kidney Cancer Association, Chicago, IL

1998 "Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D"
Johnson, Tweardy, Grandis, Steinman Laboratory Group

1998 "Nuclear matrix Proteins and Cancer Diagnosis"
Ortho-Clinical Diagnostics, Rochester, NY

1998 "Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D"
Life Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA

1998 "Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D"
Department of Urology, Northwestern University School of Medicine, Chicago, IL

1997 Second International Workshop on Diagnostic and Prognostic Markers in Bladder Cancer, Barcelona, Spain

1998 "The Effects of Vitamin D on Prostatic Growth and Neoplasia" and
"The Nuclear Matrix and Cancer"
Visiting Professorship, Department of Urology,
University of Iowa, Iowa City, IA

1998 "Utilization of the Bladder Cancer Specific Nuclear Matrix Protein, BLCA-4, for the Detection of Bladder Cancer" Society for Basic Urologic Research Fall Symposium, Prouts Neck, ME

1998 "Effects of Vitamin D on Prostate Development and Neoplasia"
New Research Approaches in the Prevention m-d Cure of Prostate Cancer, American Association for Cancer Research Special Conference in Cancer Research, Palm Springs, CA

1999 "Approaches to Prostate and Bladder Cancer: Nuclear Matrix and Vitamin D" Oncology Center, Grand Rounds, University of Wisconsin, Madison, WI

1999 Chair, Think-Tank Workshop on Prostate Cancer
Pittsburgh, PA

1999 "The Nuclear Matrix and its Role in Cancer"
Joint Graduate Program, University of Minnesota, Minneapolis, MN

1999 "Cancer Associated Nuclear Matrix Proteins"
Department of Biology, SUNY at Buffalo, Buffalo, NY

1999 "Nuclear Matrix Proteins as Markers of Cancer"
Tumor Marker Conference, Santa Barbara, California

1999 "Nuclear Matrix and Cancer"
Igen International, Inc., Gaithersburg, MD

1999 "Nuclear Matrix and Cancer"
DiaDexus, San Jose, California

1999 "Prostate Cancer"
UPMC Health News Broadcast –WQED 13
Pittsburgh, PA

1999 "The Future of Prostate Cancer: Research Horizons"
A Symposium on Prostate Cancer
NAACP – Pittsburgh, PA

1999 Panelist, National Cancer Institute
"Strategies for Developing New Clinical Trials for Prostate Cancer Chemoprevention"
Baltimore, MD

1999 "Nuclear Matrix Proteins as Biomarkers of Prostate Cancer"
NCI Prouts Neck Prostate Cancer Symposium
Prouts Neck, ME

1999 "Nuclear Matrix Proteins as Biomarkers of Cancer"
Bayer Diagnostics, Tarrytown, N.Y.

1999 "Effects of Vitamin D on Prostate Growth, Differentiation and Neoplasia"
3rd World Congress on Urological Research
Paris, France

1999 "Efficacy of a Synthetic Lytic Peptide in the Treatment of Prostate Cancer"
Joint Annual Meeting New England and Northeastern Sections of the
American Urological Association
Bermuda

1999 Visiting Professor – Department of Urology
University of Medicine & Dentistry of N.J.
New Brunswick, NJ

2000 "Diagnostics/Markers/Surrogate/Endpoints"
State of the Science Workshop on Superficial Bladder Cancer
Bethesda, MD

2000 "Nuclear Matrix Proteins as Biomarkers of Cancer"
Special Lecturer, Department of Urology
Kyoto University, Graduate School of Medicine
Kyoto, Japan

2000 "Efficacy of a Synthetic Lytic Peptide in the Treatment of Prostate Cancer"
Annual Meeting American Urological Association
Atlanta, Georgia

2000 "Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer"
Annual Meeting American Urological Association
Atlanta, Georgia

2000 "Novel Nuclear Matrix Proteins as Urinary Biomarkers"

Interstitial Cystitis Meeting
Minneapolis, MN

2000 Joint Intergroup Specimen Banking Committee Meeting
Chantilly, VA

2000 Breakout Session Chair, SOTS Workshop on Superficial Bladder Cancer
Bethesda, MD

2000 "The Novel Marker BLCA-4 for the Detection of Bladder Cancer"
Nordic Urology Association Meeting
Stockholm, Sweden

2000 Workshop on the "Mechanisms of Tumor Metastasis to the Bone: Challenges and Opportunities"
Bethesda, MD

2001 "Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer"
2nd Tumor Markers Conference
Santa Barbara, CA

2001 "Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer"
3rd Annual GU Conference
Nemacolin Woodlands / Farmington, PA

2001 "Novel Findings in Cancer Diagnosis and Treatment"
Pacific West Cancer Foundation/NCC
Miami, FL / Nassau

2001 "Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer"
European 14th IFCC Congress EUROMEDLAB 2001
Prague,Czech Republic

2001 "Approaches of Prostate and Bladder Cancer: Nuclear Structure and Vitamin D"
UroGenesys, Inc. Santa Monica, CA

2001 "Novel Technological Applications to Urologic Research"
14th Annual Spring Meeting – Society for Basic Urological Research
Anaheim, CA

2001 "Molecular Differentiation of Histologic and Symptomatic BPH"
Annual Meeting American Urological Association
Anaheim, CA

2001 "A Novel Highly Specific and Sensitive Urine-Based Assay for the Detection of Bladder Cancer"
Presentation-Eichrom
Anaheim, CA

2001 "Utilization of a Urine Based Assay for BLCA-4 in the Detection of Bladder Cancer"
AACC/CSCC 2001-Annual Meeting & Clinical Lab Expo
Chicago, IL

2001 "Nuclear Matrix Proteins as Cancer Biomarkers"
FASEB Summer Research Conference
Saxtons River, Vermont

2001 "Approaches to Prostate and Bladder Cancer: Novel Tumor Biomarkers and Vitamin D".
Millennium Pharmaceuticals, Cambridge, Massachusetts

2001 "Men's Health Issues in Basic Urologic Research"
Society for Basic Urologic Research/European Society of Urologic Research Symposium
4th World Congress in Urologic Research
Tuscon, Arizona

2001 "New Discoveries in Prostate Cancer Biology and Treatment"
AACR/Special Conference in Cancer Research
Naples, Florida

2001 Second Annual EDRN Scientific Workshop
Seattle, Washington

2002 International Bladder Symposium
Washington, D.C.

2002 "A Novel Highly Specific and Sensitive Urine-Based Assay for the Detection of Bladder Cancer"
XVIIth Congress of the European Association of Urology
Birmingham, England

2002 "Molecular Imaging in Cancer: Linking"
AACR Special Conference in Cancer Research
Lake Buena Vista, Florida

2002 "Nuclear Matrix Proteins as Cancer Biomarkers"
Georgetown University Medical Center/Department of Cell Biology
Washington, DC

2002 GU SPORE Bladder Cancer Intergroup Meeting
Houston, TX

2003 "Nuclear Matrix Proteins as Cancer Biomarkers"
The University of Texas/MD Anderson Cancer Center
Houston, Texas

2002 "A Highly Specific and Sensitive Urine-based Assay for the Detection of Bladder Cancer"
AACC/34th Annual Oak Ridge Conference /Cancer Detection and Monitoring
La Jolla, California

2002 "Nuclear Matrix Proteins – Clinical Use in Bladder Cancer"
ESUR/3rd International Conference on Prostate Cancer Research
Trento, Italy

2003 "Nuclear Structure and Cancer"
FASEB Summer Research Conference
Saxtons River, Vermont

3. Other research related activities

1992 – 1994	Donald S. Coffey Lectureship Committee Society for Basic Urologic Research
1996	Editor, "Cell Structure and Signaling" Advances in Molecular and Cellular Biology, JAI Press, Greenwich, CT
1997	Ad-hoc Member, Cell Biology Study Section American Cancer Society
1997	Member, Study Section – Special Emphasis Panel in Urology, NIDDKD, DRG, National Institutes of Health
1997	Special Emphasis Panel Program Project Review Committee, "Bone Cell Structure and Gene Expression", NIAMS, National Institutes of Health
1997 – Present	Member, Education Committee American Association for Cancer Research
1998 - Present	Cell Biology Study Section, USAMRMC (DOD) Prostate Cancer Research Program
1998	Member, Study Section – Special Emphasis Panel – Urology Research Centers, NIDDKD, DRG, National Institutes of Health
1998 – 2002	Member, Society for Basic Urologic Research Symposium Organizing Committee
1998 – Present	Editorial Board, Urologic Oncology Survey Section Urologic Oncology
1998	Co-Chairperson, Poster Discussion Session, "Molecular Markers for Cancer Susceptibility" American Association for Cancer Research 1998 Annual Meeting
1998 – 2000	Ad-Hoc Member, Executive Board Society for Basic Urologic Research
1998 – 1999	Member, Planning Committee NCI Prouts Neck Prostate Cancer Symposium
1998 – Present	Member, Prostate Research Review Committee Veterans Health Administration
1999	Member, Research Enhancement Award Program Review Committee Veterans Health Administration
1999 – 2003	Treasurer

	Society for Basic Urologic Research
1999 – 2002	Member, Peer Review Committee on Cell Structure and Metastasis. American Cancer Society
1999 - 2000	Ad-Hoc Member, NIH, National Institutes of Health, Metabolic Pathology Study Section
2000 - Present	Ad-Hoc Member, NCI, National Cancer Institute, PO1 Review Committee
2000 - Present	Member, Editorial Board, The Prostate
2001 – Present	Member, Metabolic Pathology Study Section – Oncological Sciences Integrated Review Group – Center for Scientific Review
2001	Co-Director - FASEB Summer Research Conference "Nuclear Structure and Cancer" Saxtons River, Vermont
2001	Co-Director, AACR Conference: New Discoveries in Prostate Cancer Naples, FL
2001 - Present	Editor – Molecular Oriented Basic Science Section Gold Journal - *UROLOGY*
2002	Director, Prouts Neck Prostate Cancer Meetings

4. Scientific Reviewer

Cancer Research
Journal of Cellular Biochemistry
Journal of Urology
Urology
Gold Journal - *Urology*
Experimental Cell Research
Veterans Affairs Research Command
Henry Ford Health Sciences Center
Journal of Clinical Investigation
Cancer Investigation
Journal of the National Cancer Institute
Journal of Cell Science
The Prostate
Urologic Oncology
IUBMB Life
Cancer Chemotherapy and Pharmacology
Cancer Detection and Prevention

LIST OF CURRENT RESEARCH INTERESTS:

1. Characterization of differences in nuclear matrix proteins between normal and transformed prostate, bladder and kidney cells. Identifying their role in transformation and the possibility of using these

nuclear matrix proteins as diagnostic tools and potentially as therapeutic targets.

2. Examination of the role of the nuclear matrix ill the regulation of tissue specific gene expression, focusing on androgen regulated gene expression.

3. Elucidating the role of the nuclear matrix in transcriptional regulation of gene expression.

4. Investigating the role of vitamin D in the normal prostate and in the treatment of prostate cancer.

SERVICE:

1. University and Medical School

1990	Student Representative – Search Committee for Selection of the Dean, Johns Hopkins University School of Medicine
1990 – 1991	Member, Rutgers Alumni Association Board of Directors
1994	Presentation to Wilkinsburg Kiwanis Club on PCI and Prostate Cancer
1995 – Present	Editorial Board, UPCI Clinical News
1995 – 1996	Member, UPCI Internet Committee
1996	Presentation to Parkway West Rotary Club on UPCI and Prostate Cancer
1997 – Present	Member, UPCI Annual Scientific Retreat Committee
1997 – Present	Chair, PUCC Search Committee
1997 – Present	Chair, PUCC Pilot Projects Program
1997 – Present	Member, Molecular Oncology, UPCI Search Committee
1997 – Present	Member, Urologic Oncology Search Committee
1998 – Present	Co-Chair, Recruitment Committee The Integrated Program in Biomedical Sciences University of Pittsburgh School of Medicine
1998	Presentation to USTOO Prostate Cancer Support Group at Allegheny General Hospital
1998 – Present	Member, UPCI Information Systems Steering Committee
1999	Presentation to Men's Club, Temple Ohav Shalom on UPCI and Prostate Cancer
1999	Presentation to USTOO Prostate Cancer Support Group at UPMC

1999	Presentation to Kidney Cancer Association, Pittsburgh, PA
1999-2000	Chair, Recruitment Committee The Integrated Program in Biomedical Sciences, University of Pittsburgh School of Medicine
2000 – Present	Entrepreneurial Oversight Committee University of Pittsburgh School of Medicine
2000 – Present	Member – Radiation Safety Committee
2001	Presentation to UPCI Scientific Advisory Council Meeting
2001 - 2004	Member – University of Pittsburgh Technology Transfer Oversight Committee
2002	Foundations Course Advisory Committee/University of Pittsburgh

2. Community activities

1994 - 1997	Vice-President, Franklin Ridge Community Service Association Board of Directors
1997 – 1998	President, Franklin Ridge Community Service Association Board of Directors
1998 – 1999	Secretary, Franklin Ridge Community Service Association Board of Directors

3. Continuing Medical Education (CME) activities.

APPENDIX A

facsimile TRANSMITTAL

to: Steven Maebius
Foley and Lardner

fax #: (202) 672-5399

re: Patent Information

date: October 18, 1995

pages: 24, including this cover sheet.

Dear Steve:

As you requested, enclosed is a copy of the manuscript that we are submitting to Cancer Research. This includes the table that we talked about (Table 2) and the grant information that we referenced.

Please let me know if you need any additional information.

Thanks.

From the desk of...

Robert H. Getzenberg, Ph.D.

University of Pittsburgh Cancer Institute
200 Lothrop Street - BST E1056
Pittsburgh, PA 15213-2582

(412) 383-8923
Fax: (412) 383-8928

CONFIDENTIAL

Bladder Cancer Associated Nuclear Matrix Proteins[1]

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University of Pittsburgh Cancer Institute
Prostate and Urologic Cancer Center
Departments of Pathology [R.H.G., A.K., M.J.B.], Surgery [R.H.G., B.R.K., R.R.B.], Medicine [R.H.G.] and Pharmacology [R.H.G.]
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(412) 383-8923
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Running Title: Bladder Cancer Nuclear Matrix

Key Words: Nuclear Matrix, Bladder, Nuclei, Tumor Marker, Cancer

[1]This work was supported in part by developmental funds of the University of Pittsburgh Cancer Institute and NIH grant P30 CA47904 to the University of Pittsburgh Cancer Institute.
[2]To whom requests for reprints should be addressed, at University of Pittsburgh Cancer Institute, 200 Lothrop Street, BST E-1056, Pittsburgh, PA 15213-2582

Abstract

The early diagnosis of bladder cancer is central to the effective treatment of the disease. Currently there are no methods available to easily and specifically identify the presence of bladder cancer cells. The prevailing method for the detection of bladder cancer is to identify bladder cancer cells by morphological examination of exfoliated cells or biopsy material by a pathologist. A hallmark of the malignant or transformed phenotype is abnormal nuclear shape, the presence of multiple nucleoli and altered patterns of chromatin organization. Nuclear structural alterations are so prevalent in cancer cells that they are commonly used as markers of transformation for many types of cancer. Nuclear shape is determined by the nuclear matrix, the dynamic skeleton of the nucleus. The nuclear matrix is the structural component of the nucleus that determines nuclear morphology, organizes the DNA in a three-dimensional fashion that is tissue specific, and has a central role in the regulation of a number of nuclear processes including the regulation of DNA replication and gene expression. Previous investigations into prostate and breast cancer have revealed that the nuclear matrix protein composition undergoes alterations with transformation and that the nuclear matrix can serve as a marker for the malignant phenotype. In this study, we have identified nuclear matrix proteins with which it is possible to differentiate human bladder tumors from normal bladder epithelial cells. We examine the nuclear matrix protein composition of 17 matched tumor and normal samples from patients undergoing surgery for bladder cancer. We have identified six proteins present in all tumor samples that are not present in the corresponding normal samples and three proteins that are unique to the normal bladder tissues in comparison to the tumor samples. Five of the six bladder cancer associated proteins were also identified in three human bladder cancer cell lines examined (253j, UMUC-2, T24). We have therefore, demonstrated that

nuclear matrix composition is able to differentiate bladder cancer from normal bladder tissue and may provide useful tools for early detection and recurrence of the disease. Importantly, these markers may provide valuable tools for cytopathologic screening for bladder carcinoma.

Introduction

The nuclear matrix is the framework of the nucleus and consists of the peripheral lamins and pore complexes, an internal ribonucleic protein network, and residual nucleoli (1). The nuclear matrix proteins represent approximately 10% of all nuclear proteins and are virtually devoid of lipids, DNA and histones (2). It has been demonstrated to play a central role in the regulation of important cellular processes such as DNA replication and transcription (3).

These structural components of the nucleus are known to have a central role in the specific topological organization of DNA. DNA in the nucleus is not randomly organized and although approximately ten percent of the DNA actually encodes proteins, only specific genes are positioned in a manner that permits the expression of both housekeeping and cell type specific genes. The DNA has many forms of higher order structure, including topological organization by the nuclear matrix that gives rise to a tissue specific pattern of organization that results in the expression of appropriate tissue specific genes.

A cellular hallmark of the transformed phenotype is abnormal nuclear shape and the presence of abnormal nucleoli. Nuclear structural alterations are so prevalent in cancer cells that they are commonly used as pathologic markers of transformation in many types of cancer. Nuclear shape is thought to reflect the internal nuclear structure and processes and is determined, at least in part, by the nuclear matrix (4).

Most known nuclear matrix proteins (NMPs), are common to all cell types and physiologic states. Numerous NMPs have been identified which may be unique to certain cell types or states (reviewed in 3). Mitogenic stimulation and the induction of differentiation have been demonstrated to alter the composition of nuclear matrix proteins and structure (5,6). The nuclear matrix contains

a number of associated proteins that have been demonstrated to be involved in transformation. Berezney first showed that the nuclear matrix is altered in transformation, examining hepatoma nuclear matrix proteins (7). Fey and Penman demonstrated that tumor promoters induce a specific morphologic signature in the nuclear matrix-intermediate filament scaffold of kidney cells (8), and that the pattern of NMPs differed between normal and tumorigenic cell lines (9).

We have previously characterized nuclear matrix proteins that are able to serve as markers to differentiate prostate cancer from normal prostate in both a rat model system (10) and in human prostate samples (11). In addition, NMP composition was able to be utilized to distinguish between metastatic and non-metastatic tumors (10). NMPs have also been identified to be associated with human breast cancer that are not found in normal breast tissue (12). Recently, an antibody to a nuclear matrix protein, termed NM-200.4, was raised from the breast carcinoma cell line T-47D (13). This antibody reacts strongly with human breast carcinoma specimens as well as specimens from lung, thyroid, and ovarian cancers, but does not react with normal epithelial cells of similar origin, this suggests that certain anti-NMP antibodies may be developed as diagnostic tools. The strong evidence linking changes in the nuclear matrix with cancer has led to the suggestion that the nuclear matrix might serve as an excellent target for anti-cancer agents (14).

These data provide a strong rationale for investigation of the differences in NMP composition that may be discerned in normal versus transformed bladder tissue. We have compared the protein composition of the nuclear matrix in bladder tumors with adjacent normal bladder tissue from these individuals as well as to normal bladder samples obtained from organ donors. In addition, we examined the NMP composition of several human bladder cancer cell lines. We identified six NMPs that are found in the tumor samples that are not present in the normal tissues and three NMPs that

are identified in the normal tissue but are absent in the tumors. Five of the six cancer specific NMPs were also found in all of the bladder cancer cell lines.

Methods and Materials

CELL LINES AND TISSUE PROCESSING.

Matched normal and tumor bladder tissue samples were obtained from patients undergoing surgery for bladder cancer at the University of Pittsburgh Medical Center. All patients had Transitional Cell Carcinoma. The tumor samples collected were of the following clinical stage according to the AJCC (15). Six of the tumors were T_{is}-T_1, eight were T_3, and three were T_4 (see Table 1 attached). The TNM histopathologic grade of the lesions revealed four, G1 (well differentiated) tumors, two G2 (moderately differentiated) tumors and eleven G3 lesions (poorly or undifferentiated) (16, 17). In addition to TNM staging and grading, the tumors were graded according to Bergkvist's classification (16). None of the lesions were grade 1, seven were grade 2, nine were grade 3 and one was grade 4. Normal bladders were obtained from the Center for Organ Recovery and Education (CORE). Only samples that could be clearly identified by the pathologist as containing approximately pure populations of the stated tumor grade were utilized. The cell lines (253j, UMUC-2, T24) were kindly provided by Dr. Monica Liebert, University of Texas MD Anderson Cancer Center (Houston, TX) and grown in RPMI 1640 (Life Technologies, Rockville, MD) with 10% fetal bovine serum (Life Technologies, Rockville, MD).

NUCLEAR MATRIX PREPARATION

The nuclear matrix is defined as the residual components of the nucleus which are insoluble

to a series of detergent and salt extractions following DNase treatment (1). The isolation procedure utilized in these experiments involves the release of cytoskeleton proteins by the use of a mild salt extraction with 0.25 M ammonium sulfate of detergent treated nuclei that no longer possess their membrane lipid components. This is followed by DNase I and RNase A treatment to remove chromatin structures. This extraction causes minimal disruption of the NMPs and nuclear matrix structure (8,18).

The nuclear matrix proteins were isolated from bladder tissue and tumors, according to our previously published adaptation of the methodology of Fey and Penman (10,18). Briefly, the tissue pieces were minced into small (1mm^3) pieces and homogenized with a Teflon pestle on ice with 0.5% Triton X-100 in a solution containing 2 mM vanadyl ribonucleoside (RNase inhibitor) to release the lipids and soluble proteins. Extracts were then filtered through a 350 micron nylon mesh and extracted with 0.25 M ammonium sulfate to release the soluble cytoskeletal elements. DNase treatment at 25°C was used to remove the soluble chromatin. The remaining fractions contain intermediate filaments and nuclear matrix proteins. This fraction was then disassembled with 8 M urea, and the insoluble components, which consist principally of carbohydrates and extracellular matrix components, were pelleted. The urea was dialyzed out, and the intermediate filaments were allowed to reassemble and subsequently removed by centrifugation. The nuclear matrix proteins were then ethanol precipitated. All solutions contained freshly prepared 1 mM phenylmethylsulfonylfluoride (PMSF) to inhibit serine proteases, 0.3 µM aprotonin, 1 µM leupeptin and 1 µM pepstatin. Dr. Sheldon Penman (Massachusetts Institute of Technology, Cambridge, MA) has prepared antibodies to proteins of this fraction and demonstrated that they are localized exclusively in the nucleus and isolated nuclear matrix fraction. The protein composition

was determined by resuspending the proteins and utilizing the Coomassie Plus protein assay reagent kit (Pierce, Rockford, IL) with bovine serum albumin (BSA) as a standard. For gel electrophoresis, the ethanol precipitated NMPs were dissolved in a sample buffer consisting of 9 M urea, 65 mM 3-[(3-Cholamidopropyl)-dimethyl-ammonio]-1-propanesulfonate (CHAPS), 2.2% ampholytes and 140 mM dithiothreitol (Oxford Glycosystems, Bedford, MA). The final pellet containing NMPs represented less than 1% of the total cellular proteins.

HIGH RESOLUTION TWO-DIMENSIONAL ELECTROPHORESIS

High resolution two-dimensional gel electrophoresis was carried out utilizing the Investigator 2-D gel system (Oxford Glycosystems, Bedford, MA) (19) as previously described (10). Briefly, one-dimensional isoelectric focusing was carried out for 18,000 V-hours using 1-mm x 18-cm tube gels after 1.5h of prefocusing. The tube gels were extruded and placed on top of 1-mm sodium dodecyl sulfate Duracryl (Oxford Glycosystems, Bedford, MA) high tensile strength polycarylamide electrophoresis slab gels, and the gels were electrophoresed with 12°C constant temperature regulation for approximately 5 hours. Gels were fixed with 50% methanol and 10% acetic acid. After thorough rinsing and rehydration, gels were treated with 5% glutaraldehyde and 5 mM dithiothreitol after buffering with 50 mM phosphate (pH 7.2). The gels were stained with silver stain using the methodology of Wray et al. (20) (Accurate Chemical Co., Inc., Westbury, NY). Fifty micrograms of nuclear matrix protein were loaded for each gel. Protein molecular weight standards were Silver Standards from Diversified Biotechnology (Newton Centre, MA). Isoelectric points were determined using BDH carbamylated standards (Gallard-Schlesinger, Carle Place, NY) and Sigma Chemical Co. (St. Louis, MO). Multiple gels were run for each sample, and multiple samples

run at different times. Only protein spots clearly and reproducibly observed in all the gels of a sample type were counted as actually representing the nuclear matrix components. The gels were analyzed using the BioImage 2D Electrophoresis Analysis System (BioImage, Ann Arbor, MI) which matches protein spots between gels and databases the gels and protein spots.

Results

We have obtained tumor and normal tissue from seventeen matched bladder samples. NMPs have been extracted and separated by high resolution two-dimensional gel electrophoresis. The NMP composition of the 17 tumors and their corresponding normal tissue were then analyzed utilizing a computer based gel analysis system. All tumors contain differences in their nuclear matrix composition when compared to the nuclear matrix composition of the matched normal tissue from the same bladder. Consistent differences were noted for all of the samples. An example of the NMP composition of a bladder tumor and normal bladder tissue is presented in figure 1. There are several notable differences in nuclear matrix composition in the bladder tumor when compared to the normal tissue. We have identified six proteins (BLCA-1 to BLCA-6) that are present in all of the tumors and are absent in the normals (Figure 1B) and three proteins (BLNL-1 to BLNL-3) that are found in all of the normal bladder tissue samples (Figure 1A) and are missing in the tumor samples (Figure 1 and Table 2). These differences appear to be unique to bladder cancer in that the molecular weights and isoelectric points of the proteins do not appear to correspond to those proteins previously reported to be different in prostate and breast cancers (Table 2). In addition, we have now examined several normal human bladders to further our investigations into the NMP composition of normal bladder tissue. We have relatively large numbers of these normal bladders

which will allow us the study, in detail, changes that occur in NMPs during the transformation from normal cell to bladder cancer. While these comparisons are still in the preliminary stage, it appears that the nuclear matrix composition of these normal bladders contains the three normal specific proteins and does not contain the tumor specific proteins.

The tumor samples that we examined are complex mixtures of epithelial, stromal, immunological and other cell types. In order to determine if the nuclear matrix changes that we were detecting actually represented changes that were occurring in the neoplastic transitional cell, we examined the NMP composition of several bladder cancer cell lines. The human bladder cancer lines, 253j, T24 and UMUC-2 were grown and their nuclear matrix proteins isolated. These NMPs were then separated by 2-D electrophoresis and silver stained. As demonstrated in Figure 2, of the six NMPs determined to be found only in the bladder tumors samples, 5 of these proteins were identified in the three cell lines. Only the protein BLCA-5 was not identified in the three cell lines. None of the proteins found only in normal bladder samples (BLNL-1 - BLNL-3) were found in these lines.

Discussion

The nuclear matrix is the binding site for tumor associated proteins, including the myc oncogene product, adenovirus E1A-transforming protein, polyoma large T antigen, and the Tat protein from human immunodeficiency virus type 1 (HIV-1) (21-24). Changes in expression of a nuclear matrix associated protein in NIH3T3 cells have been found in oncogene transformed cells (25). The monoclonal antibody Ki-67, typically used to identify proliferating cells, has been demonstrated to be directed against a nuclear matrix protein (26). The nuclear matrix has also been

demonstrated to be the preferential binding target of the carcinogen benzo[a]pyrene (27).

Previous investigations have investigated how the nuclear matrix is altered in cancer cells, and have shown that these matrix protein patterns can distinguish closely related sublines of the same Dunning tumor. The nuclear matrix proteins in several Dunning cell lines were examined and compared with the nuclear matrix protein composition of the dorsal prostate, the original tissue from which this tumor was derived. Using high resolution two-dimensional gel electrophoresis, the NMPs of the Dunning cell lines were found to be significantly different from that of the rat dorsal prostate. A minimum of ten abundant spots were identified as unique to the rat dorsal prostate when compared with the Dunning lines i.e., they were absent in the tumor cells (10). Similarly, there were several proteins which were unique to the Dunning cell lines that were absent in the dorsal prostate nuclear matrix. When the NMP patterns of the Dunning cell lines were compared with one another, they appeared relatively similar in protein composition. The AT-2 and MLL cell lines were alike in their protein composition of the relatively abundant proteins. However, these two cell lines did contain two proteins which were not found in the G cell line. Conversely, the nuclear matrix of the G cell line exhibited two unique proteins which were not present in the AT-2 or MLL cells (10).

We have recently completed a study on the NMP composition in human prostate tissue (11). We compared the NMP patterns in fresh normal prostate, benign prostatic hyperplasia (BPH), and prostate cancer from 21 men undergoing surgery for clinically localized prostate cancer or BPH. Onc protein (PC-1), a M_r 56,000 protein with an isoelectric point of 6.58, appeared in all of 14 nuclear matrix preparations from different prostate cancer specimens and was not detected in normal prostate (0 of 13) or BPH (0 of 14). This protein is currently being investigated as a possible diagnostic tool for prostate cancer. We have purified this protein to homogeneity and are now

sequencing this protein as well as raising antibodies to further characterize its expression.

Work from the laboratory of Pienta and colleagues has begun to determine the nuclear matrix protein composition of normal human breast tissue as well as breast tumors (12). These data were analyzed in conjunction with the nuclear matrix composition from the human breast cell lines MCF10M (mortal), MCF10A (immortal), and transfected human breast cell line MCF10AneoT. Review of 10 different tumor samples revealed at least four proteins that were expressed in tumor tissue but not in normal tissue. One protein, was a low molecular weight (18kD) protein and the others were found at relatively low isoelectric points (pI), between 60 and 80 kD. In addition, two proteins, of 24 and 26 kD, were found in the normal breast samples but, were not detected in the tumor samples. These studies, taken as a whole, suggest that the protein composition of the human breast nuclear matrix may provide insight into the biologic etiology of breast cancer and may provide biologic markers of growth and gene expression in the human breast.

Currently, the only available marker for bladder cancer identification is morphological examination of cytology samples or cystoscopic biopsies. This method is accurate for high grade lesions, however, a significant proportion of bladder tumors (25-45%) are low grade or well differentiated and escape detection upon cytologic examination of exfoliated cells. In general, the diagnostic accuracy of cytology alone for the detection of low grade transitional carcinoma is between 49 to 64 percent (if suspicious urines are considered positive) (25). The accuracy of cytology can be increased by repeating the study (26), however, this is a costly and time consuming practice for both the patient and physician. Development of a sensitive screening assay that could specifically detect bladder carcinoma would significantly enhance patient management and the early detection of bladder carcinoma. The identification of NMP(s) that indicate the presence of bladder

cancer in a sample may therefore permit development of a diagnostic test for bladder cancer. NMPs have been shown to be shed by tumors as cells die and have been demonstrated to present in the serum and urine of cancer patients (27). Therefore, it is possible that the NMP(s) described here could be utilized as markers for bladder cancer in serum or in voided urine. These markers could not only aid in the early identification of bladder cancer but also in the detection of recurrent disease. Currently, patients who have had bladder tumors removed must undergo frequent cystoscopic examinations to rule out recurrent disease. The ability to utilize a blood or urine test to identify patients with disease recurrence would greatly aid in the detection of the disease and decrease the need for these patients to have repeated cystoscopic evaluations.

Deciphering the NMPs that are either present or absent in cancer cells will provide novel information about their role in cancer and since the nuclear matrix plays a central role in DNA organization and the regulation of gene expression, these proteins may be crucial to the transformation process. Thus, these nuclear matrix proteins may serve as possible therapeutic targets.

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Figure 1

Comparison of Nuclear Matrix Proteins of Human Bladder Cancer and Normal Bladder Tissue. Silver stained high resolution two-dimensional gel electrophoresis of NMPs of (A) normal bladder tissue and (B) bladder cancer representative of the nuclear matrix patterns demonstrated in these studies.

Figure 2

Nuclear Matrix Proteins Associated with Human Bladder Cancer are Identified in Three Human Bladder Cancer Cell Lines. Silver stained high resolution two-dimensional gel electrophoresis of NMPs of the human bladder cancer cell lines 253j (A), T24 (B), and UMUC-2 (C). Identified proteins correspond to those in Figure 1, demonstrated to be found only in human bladder cancer samples.

Table 1 *Bladder Tumor Pathology*

Case Number	Nuclear Grade	TNM Stage	TNM Histo Grade
1	III	T3aN0Mx	G3
2	III	T3bN0Mx	G3
3	III	T4aNxMx	G3
4	II	TaN0Mx	G1
5	III	T3bN2Mx	G3
6	III	T4aN0Mx	G3
7	II	T4N0Mx	G1
8	III	T1N0Mx	G3
9	III	T3biN0Mx	G3
10	II	T3bN0Mx	G3
11	II	T1N0Mx	G1
12	II	T1NxMx	G1
13	IV	T3biN2M1	G3
14	III	T3bNxMx	G3
15	II	T1N0Mx	G2
16	II	T_{is}NxMx	G2
17	III	T3bN2Mx	G3

Nuclear Grade	**I**	**II**	**III**	**IV**
number of cases	0	7	9	1
T Stage	**1**	**2**	**3**	**4**
number of cases	6	0	8	3
TNM Histopathologic Grade	**G1**	**G2**	**G3**	
number of cases	4	2	11	

Table 2 *Nuclear matrix proteins which are able to differentiate normal bladder from bladder cancer samples which were identified by high resolution two-dimensional gel electrophoresis*

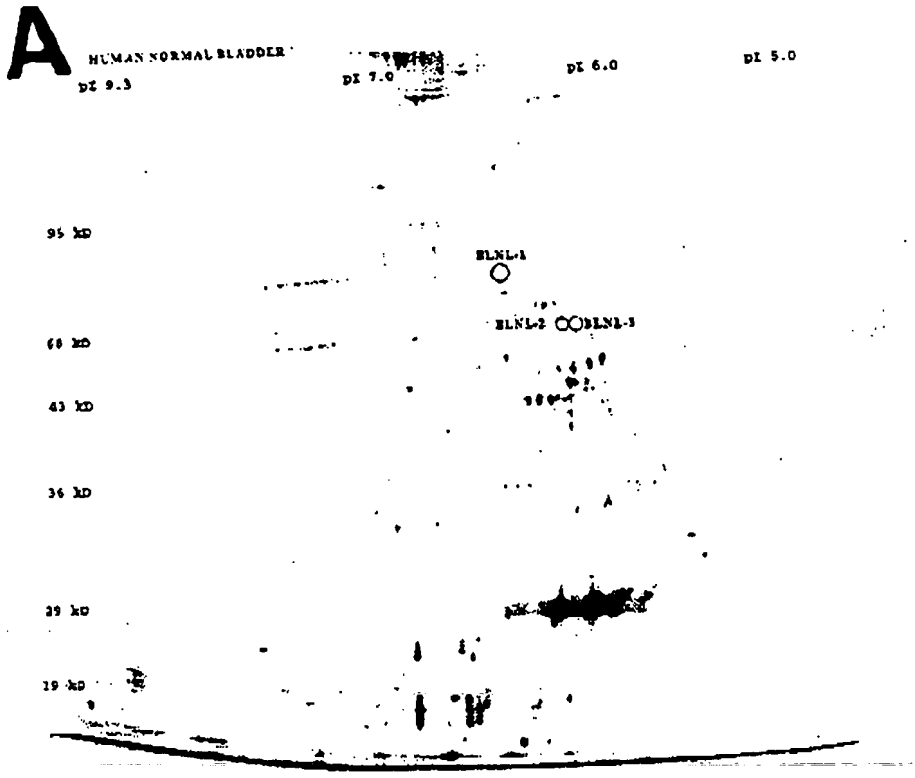
Proteins Associated with Human Bladder Cancer

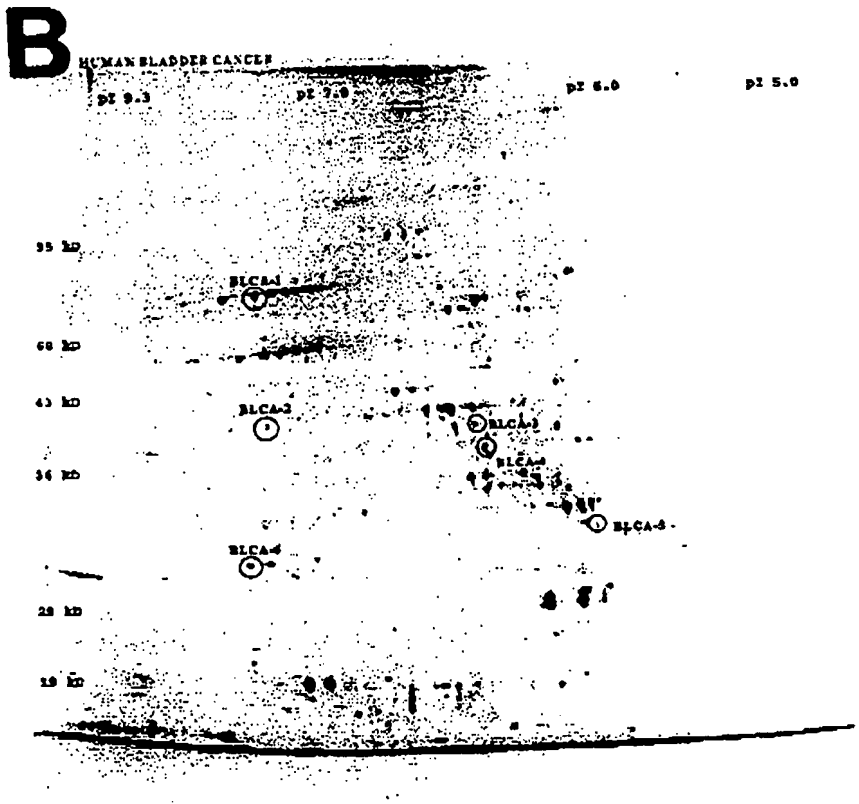
	Molecular Weight (kD)	pI
BLCA-1	72	7.70
BLCA-2	40	7.50
BLCA-3	39	6.27
BLCA-4	37	6.24
BLCA-5	29	5.80
BLCA-6	22	8.00

Proteins Associated with Normal Human Bladder

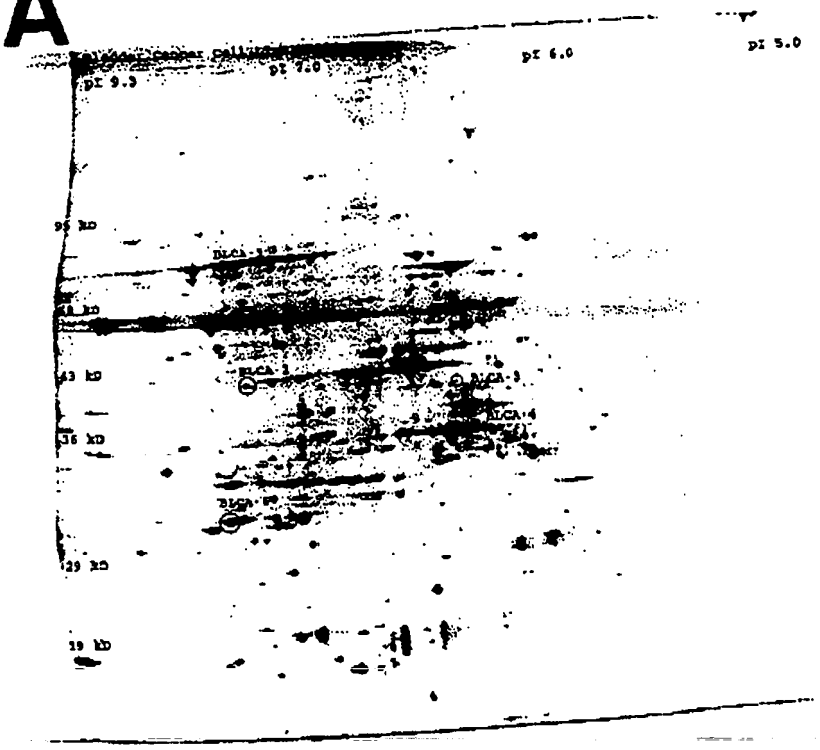
	Molecular Weight (kD)	pI
BLNL-1	70	6.09
BLNL-2	66	5.84
BLNL-3	66	5.80

The designation of each protein corresponds to the identified proteins in Figures 1 and 2. Molecular weights and isoelectric points were identified as stated in "Materials and Methods".


A
HUMAN NORMAL BLADDER
pI 9.3
pI 7.0
pI 6.0
pI 5.0
95 kD
68 kD
43 kD
36 kD
29 kD
19 kD
BLNL-1
BLNL-2
BLNL-3


B
HUMAN BLADDER CANCER
pI 9.3
pI 7.0
pI 6.0
pI 5.0
95 kD
68 kD
43 kD
36 kD
29 kD
19 kD
BLCA-1
BLCA-2
BLCA-3
BLCA-4
BLCA-5
BLCA-6

A



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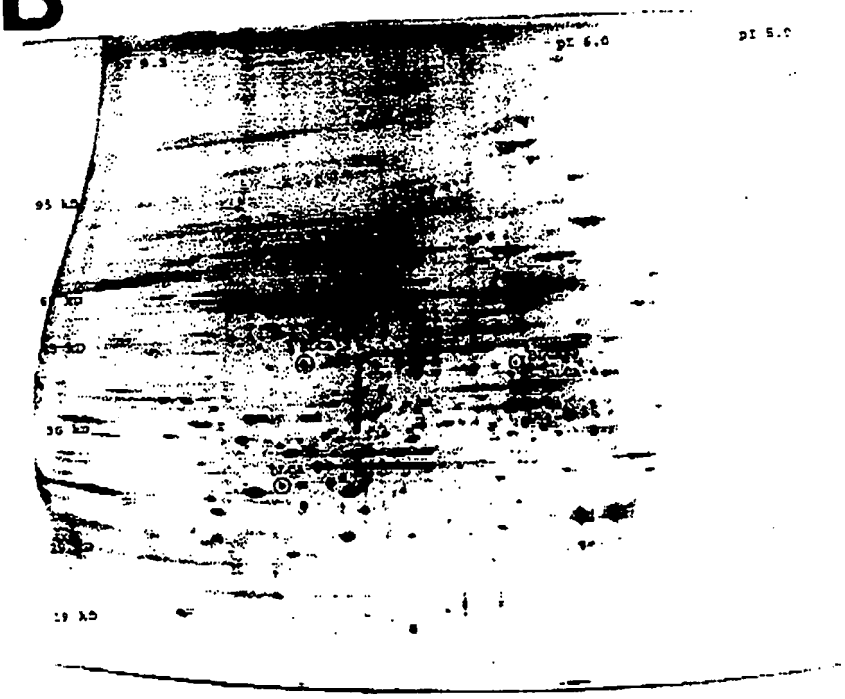
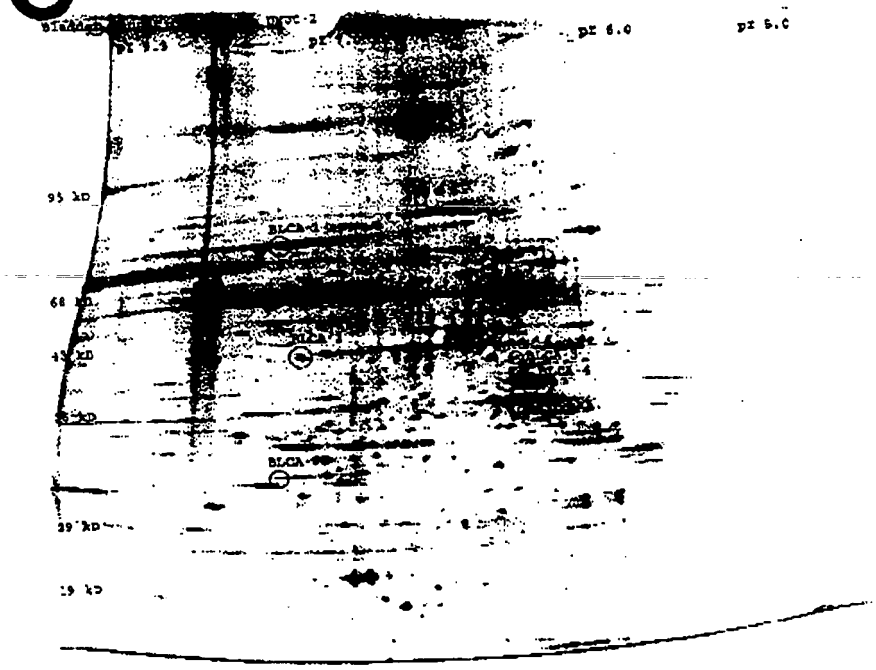


C



APPENDIX B

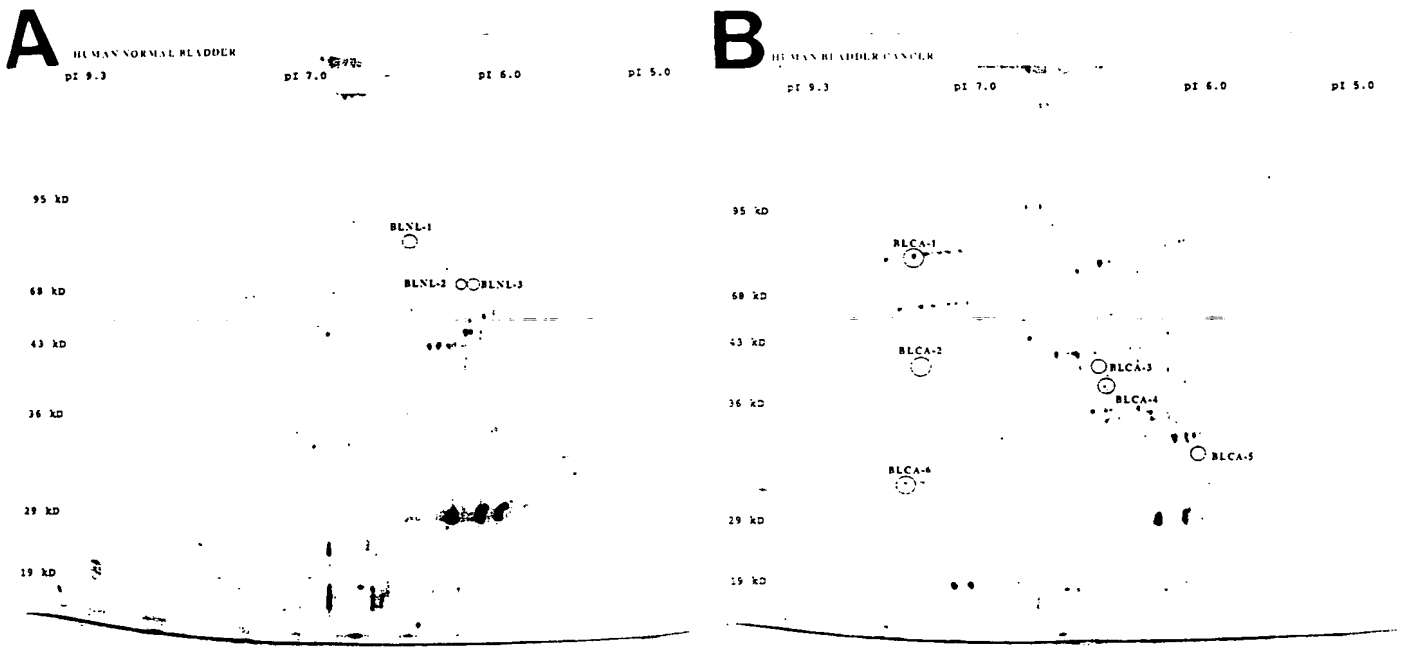


Figure 1

Comparison of Nuclear Matrix Proteins of Human Bladder Cancer and Normal Bladder Tissue. Silver stained high resolution two-dimensional gel electrophoresis of NMPs of (A) normal bladder tissue and (B) bladder cancer representative of the nuclear matrix patterns demonstrated in these studies.